

9



Muscles and Muscle Tissue

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Because flexing muscles look like mice scurrying beneath the skin, some scientist long ago dubbed them *muscles*, from the Latin *mus* meaning “little mouse.” Indeed, we tend to think of the rippling muscles of professional boxers or weight lifters when we hear the word *muscle*. But muscle is also the dominant tissue in the heart and in the walls of other hollow organs. In all its forms, muscle tissue makes up nearly half the body’s mass.

Muscles are distinguished by their ability to transform chemical energy (ATP) into directed mechanical energy. In so doing, they become capable of exerting force.

Overview of Muscle Tissues

- ✓ Compare and contrast the three basic types of muscle tissue.
- ✓ List four important functions of muscle tissue.

Types of Muscle Tissue

Chapter 4 introduced the three types of muscle tissue—*skeletal*, *cardiac*, and *smooth*. Now we are ready to describe each type in detail, but before we do, let's introduce some terminology.

- Skeletal and smooth muscle cells (but not cardiac muscle cells) are elongated, and for this reason, they are called **muscle fibers**.
- Whenever you see the prefixes **myo** or **mys** (both are word roots meaning “muscle”) or **sarco** (flesh), the reference is to muscle. For example, the plasma membrane of muscle cells is called the *sarcolemma* (sar'ko-lem'ah), literally, “muscle” (sarco) “husk” (lemma), and muscle cell cytoplasm is called *sarcoplasm*.

Okay, let's get to it.

Skeletal Muscle

Skeletal muscle tissue is packaged into the *skeletal muscles*, organs that attach to and cover the bony skeleton. Skeletal muscle fibers are the longest muscle cells and have obvious stripes called *striations* (see Figure 4.9a, p. 138). Although it is often activated by reflexes, skeletal muscle is called **voluntary muscle** because it is the only type subject to conscious control.

- When you think of skeletal muscle tissue, the key words to keep in mind are *skeletal*, *striated*, and *voluntary*.

Skeletal muscle is responsible for overall body mobility. It can contract rapidly, but it tires easily and must rest after short periods of activity. Nevertheless, it can exert tremendous power, a fact revealed by reports of people lifting cars to save their loved ones. Skeletal muscle is also remarkably adaptable. For example, your forearm muscles can exert a force of a fraction of an ounce to pick up a paper clip—or a force of about 6 pounds to pick up this book!

Cardiac Muscle

Cardiac muscle tissue occurs only in the heart (the body's blood pump), where it constitutes the bulk of the heart walls. Like skeletal muscle cells, cardiac muscle cells are striated (see Figure 4.9b, p. 139), but cardiac muscle is not voluntary. Indeed, it can and does contract without being stimulated by the nervous system. Most of us have no conscious control over how fast our heart beats.

- Key words to remember for cardiac muscle are *cardiac*, *striated*, and *involuntary*.

Cardiac muscle usually contracts at a fairly steady rate set by the heart's pacemaker, but neural controls allow the heart to speed up for brief periods, as when you race across the tennis court to make that overhead smash.

Smooth Muscle

Smooth muscle tissue is found in the walls of hollow visceral organs, such as the stomach, urinary bladder, and respiratory passages. Its role is to force fluids and other substances through internal body channels. Like skeletal muscle, smooth muscle consists of elongated cells, but smooth muscle has no striations (see Figure 4.9c, p. 139).

Like cardiac muscle, smooth muscle is not subject to voluntary control. Its contractions are slow and sustained.

- We can describe smooth muscle tissue as *visceral*, *nonstriated*, and *involuntary*.

Special Characteristics of Muscle Tissue

What enables muscle tissue to perform its duties? Four special characteristics are key.

Excitability, also termed **responsiveness**, is the ability to receive and respond to a stimulus, that is, any change in the environment either inside or outside the body. In the case of muscle, the stimulus is usually a chemical—for example, a neurotransmitter released by a nerve cell, or a local change in pH. The response (sometimes separated out as an additional characteristic called conductivity) is to generate an electrical impulse that travels along the plasma membrane of the muscle cell and causes the cell to contract.

Contractility is the ability to shorten forcibly when adequately stimulated. This ability sets muscle apart from all other tissue types.

Extensibility is the ability to extend or stretch. Muscle cells shorten when contracting, but they can stretch, even beyond their resting length, when relaxed.

Elasticity is the ability of a muscle cell to recoil and resume its resting length after stretching.

Muscle Functions

Muscle performs at least four important functions for the body. It produces movement, maintains posture, stabilizes joints, generates heat, and more.

Producing Movement

Just about all movements of the human body and its parts result from muscle contraction. Skeletal muscles are responsible for all locomotion (moving from place to place) and manipulation. They enable you to respond quickly to changes in the external environment—for example, jump out of the way of a car, direct your eyes, and smile or frown.

Blood courses through your body because of the rhythmically beating cardiac muscle of your heart and the smooth muscle in the walls of your blood vessels, which helps maintain blood pressure. Smooth muscle in organs of the digestive, urinary, and reproductive tracts propels, or squeezes, substances (foodstuffs, urine, semen) through the organs and along the tract.

Maintaining Posture and Body Position

We are rarely aware of the skeletal muscles that maintain body posture. Yet these muscles function almost continuously, making one tiny adjustment after another to counteract the never-ending downward pull of gravity.

Stabilizing Joints

Even as muscles pull on bones to cause movement, they stabilize and strengthen the joints of the skeleton (Chapter 8).

Generating Heat

Muscles generate heat as they contract. This heat is vitally important in maintaining normal body temperature. Because skeletal muscle accounts for at least 40% of body mass, it is the muscle type most responsible for generating heat.

Additional Functions of Muscle

What else do muscles do? Skeletal muscles protect the more fragile internal organs (the viscera) by enclosing them. Smooth muscle forms valves to regulate the passage of substances through internal body openings, dilates and constricts the pupils of your eyes, and forms the arrector pili muscles attached to hair follicles.



In this chapter, we examine the structure and function of skeletal muscle. Then we consider smooth muscle more briefly, largely by comparing it with skeletal muscle. We describe cardiac muscle in detail in Chapter 18, but for easy comparison, Table 9.3 on p. 310 summarizes the characteristics of all three muscle types.

✓ Check Your Understanding

1. When describing muscle, what does “striated” mean?
2. Harry is pondering an exam question that asks, “Which muscle type has elongated cells and is found in the walls of the urinary bladder?” How should he respond?

For answers, see Appendix H.

Skeletal Muscle

- ✓ Describe the gross structure of a skeletal muscle.
- ✓ Describe the microscopic structure and functional roles of the myofibrils, sarcoplasmic reticulum, and T tubules of skeletal muscle fibers.
- ✓ Describe the sliding filament model of muscle contraction.

For easy reference, **Table 9.1** on p. 283 summarizes the levels of skeletal muscle organization, gross to microscopic, that we describe in the following sections.

Gross Anatomy of a Skeletal Muscle

Each **skeletal muscle** is a discrete organ, made up of several kinds of tissues. Skeletal muscle fibers predominate, but blood vessels, nerve fibers, and substantial amounts of connective tissue are also present. We can easily examine a skeletal muscle’s shape and its attachments in the body without a microscope.

Nerve and Blood Supply

In general, one nerve, one artery, and one or more veins serve each muscle. These structures all enter or exit near the central part of the muscle and branch profusely through its connective tissue sheaths (described below). Unlike cells of cardiac and smooth muscle tissues, which can contract without nerve

stimulation, every skeletal muscle fiber is supplied with a nerve ending that controls its activity.

Skeletal muscle has a rich blood supply. This is understandable because contracting muscle fibers use huge amounts of energy and require almost continuous delivery of oxygen and nutrients via the arteries. Muscle cells also give off large amounts of metabolic wastes that must be removed through veins if contraction is to remain efficient. Muscle capillaries, the smallest of the body’s blood vessels, are long and winding and have numerous cross-links, features that accommodate changes in muscle length. They straighten when the muscle stretches and contort when the muscle contracts.

Connective Tissue Sheaths

In an intact muscle, several different connective tissue sheaths wrap individual muscle fibers. Together these connective tissue sheaths support each cell and reinforce and hold together the muscle as a whole, preventing the bulging muscles from bursting during exceptionally strong contractions.

Let’s consider these connective tissue sheaths from external to internal (see **Figure 9.1** and the top three rows of Table 9.1).

- **Epimysium.** The **epimysium** (ep’i-mis’e-um; meaning “outside the muscle”) is an “overcoat” of dense irregular connective tissue that surrounds the whole muscle. Sometimes it blends with the deep fascia that lies between neighboring muscles or the superficial fascia deep to the skin.
- **Perimysium and fascicles.** Within each skeletal muscle, the muscle fibers are grouped into **fascicles** (fas’i-klz; “bundles”) that resemble bundles of sticks. Surrounding each fascicle is a layer of fibrous connective tissue called **perimysium** (per’i-mis’e-um; meaning “around the muscle [fascicles]”).
- **Endomysium.** The **endomysium** (en’do-mis’e-um; meaning “within the muscle”) is a wispy sheath of connective tissue that surrounds each individual muscle fiber. It consists of fine areolar connective tissue.

As shown in Figure 9.1, all of these connective tissue sheaths are continuous with one another as well as with the tendons that join muscles to bones. When muscle fibers contract, they pull on these sheaths, which transmit the pulling force to the bone to be moved. The sheaths contribute somewhat to the natural elasticity of muscle tissue, and also provide entry and exit routes for the blood vessels and nerve fibers that serve the muscle.

Attachments

Recall from Chapter 8 that most skeletal muscles span joints and attach to bones (or other structures) in at least two places. When a muscle contracts, the movable bone, the muscle’s **insertion**, moves toward the immovable or less movable bone, the muscle’s **origin**. In the muscles of the limbs, the origin typically lies proximal to the insertion.

Muscle attachments, whether origin or insertion, may be direct or indirect.

- In **direct**, or **fleshy**, **attachments**, the epimysium of the muscle is fused to the periosteum of a bone or perichondrium of a cartilage.

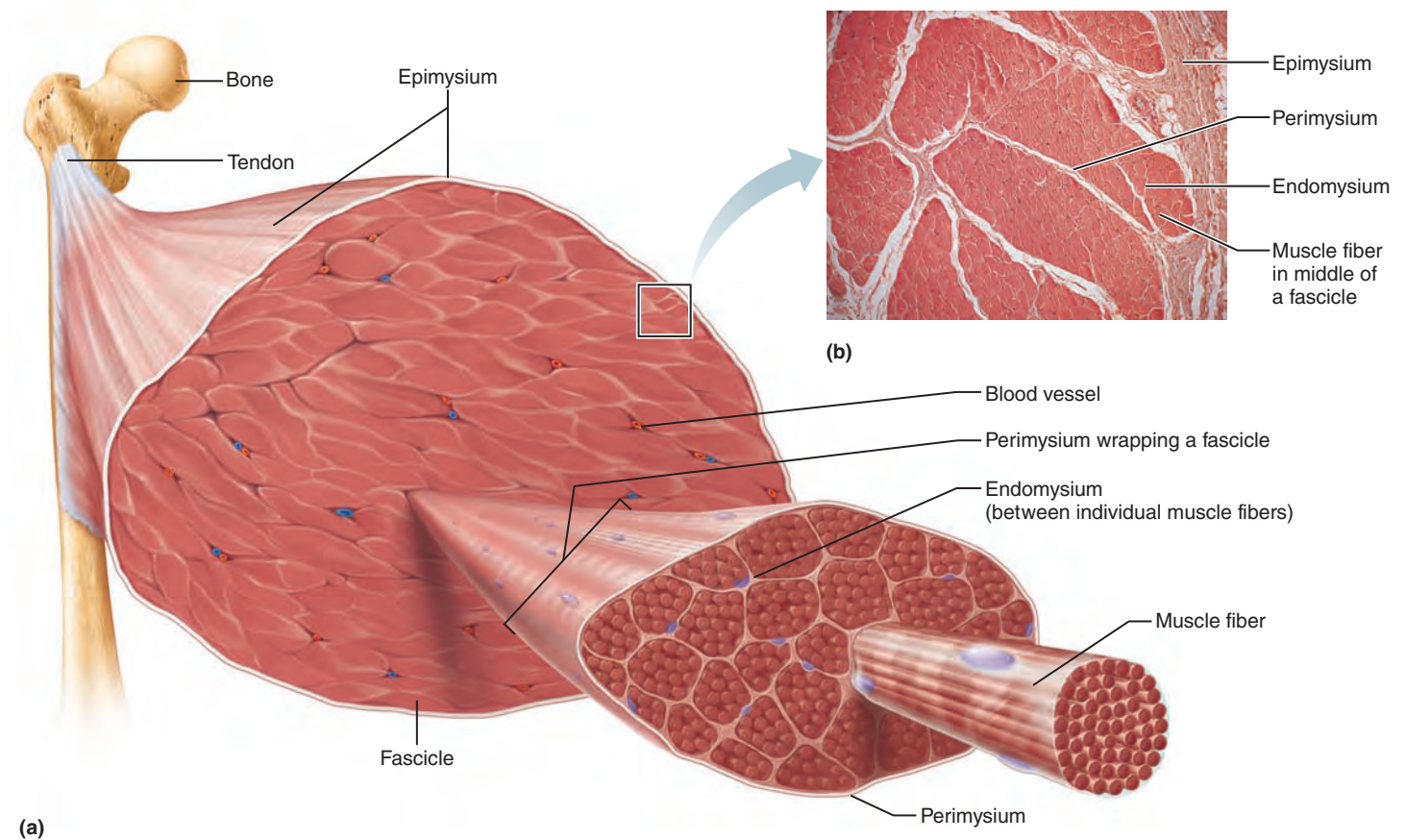


Figure 9.1 Connective tissue sheaths of skeletal muscle: epimysium, perimysium, and endomysium. (b) Photomicrograph of a cross section of part of a skeletal muscle (30 \times). (For a related image, see *A Brief Atlas of the Human Body*, Plate 29.)

- In **indirect attachments**, the muscle's connective tissue wrappings extend beyond the muscle either as a ropelike **tendon** (Figure 9.1a) or as a sheetlike **aponeurosis** (ap"o-nu-ro'sis). The tendon or aponeurosis anchors the muscle to the connective tissue covering of a skeletal element (bone or cartilage) or to the fascia of other muscles.

Indirect attachments are much more common because of their durability and small size. Tendons are mostly tough collagen fibers which can withstand the abrasion of rough bony projections that would tear apart the more delicate muscle tissues. Because of their relatively small size, more tendons than fleshy muscles can pass over a joint—so tendons also conserve space.

Before moving on to microscopic anatomy, you may want to review the top three rows of Table 9.1.

Microscopic Anatomy of a Skeletal Muscle Fiber

Each skeletal muscle fiber is a long cylindrical cell with multiple oval nuclei just beneath its **sarcolemma** or plasma membrane (Figure 9.2b). Skeletal muscle fibers are huge cells. Their diameter typically ranges from 10 to 100 μm —up to ten times that

of an average body cell—and their length is phenomenal, some up to 30 cm long. Their large size and multiple nuclei are not surprising once you learn that hundreds of embryonic cells fuse to produce each fiber.

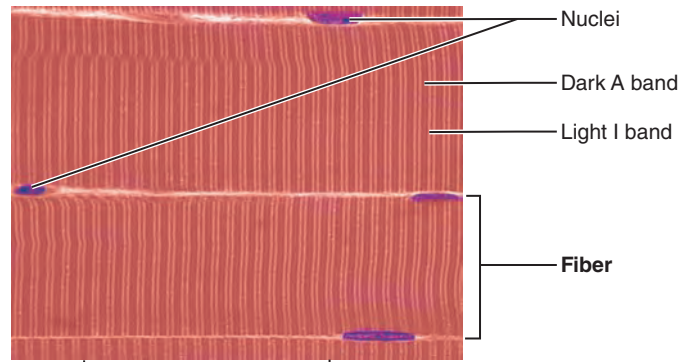
Sarcoplasm, the cytoplasm of a muscle cell, is similar to the cytoplasm of other cells, but it contains unusually large amounts of **glycosomes** (granules of stored glycogen that provide glucose during muscle cell activity) and **myoglobin**, a red pigment that stores oxygen. Myoglobin is similar to hemoglobin, the pigment that transports oxygen in blood.

In addition to the usual organelles, a muscle cell contains three structures that are highly modified: myofibrils, sarcoplasmic reticulum, and T tubules. Let's look at these structures more closely because they play important roles in muscle contraction.

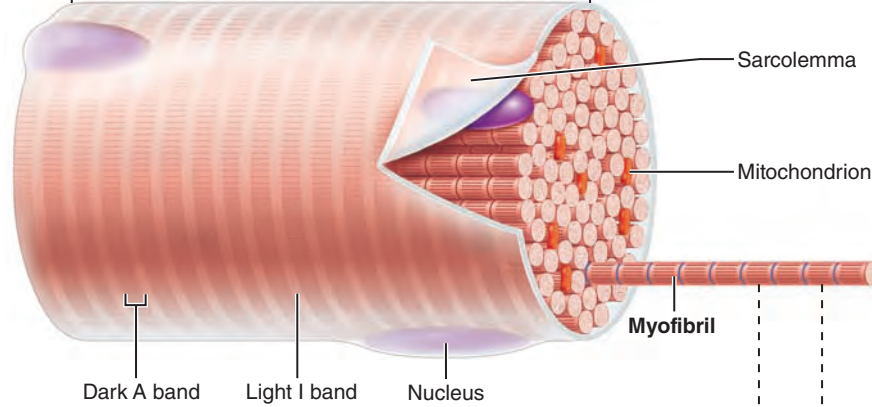
Myofibrils

A single muscle fiber contains hundreds to thousands of rod-like **myofibrils** that run parallel to its length (Figure 9.2b). The myofibrils, each 1–2 μm in diameter, are so densely packed in the fiber that mitochondria and other organelles appear to be squeezed between them. They account for about 80% of cellular volume.

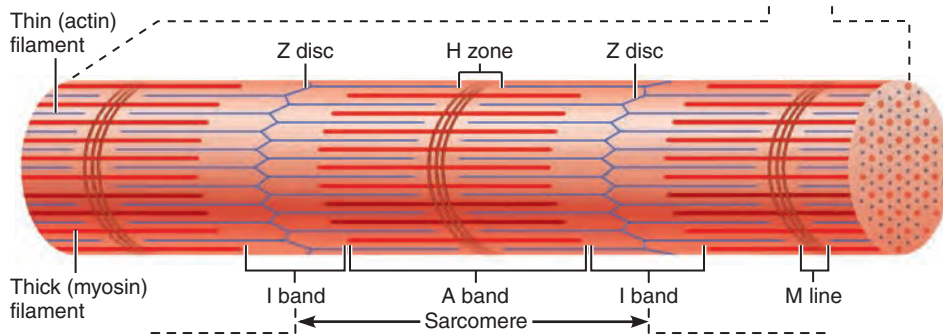
(a) Photomicrograph of **portions of two isolated muscle fibers** (700×). Notice the obvious striations (alternating dark and light bands).



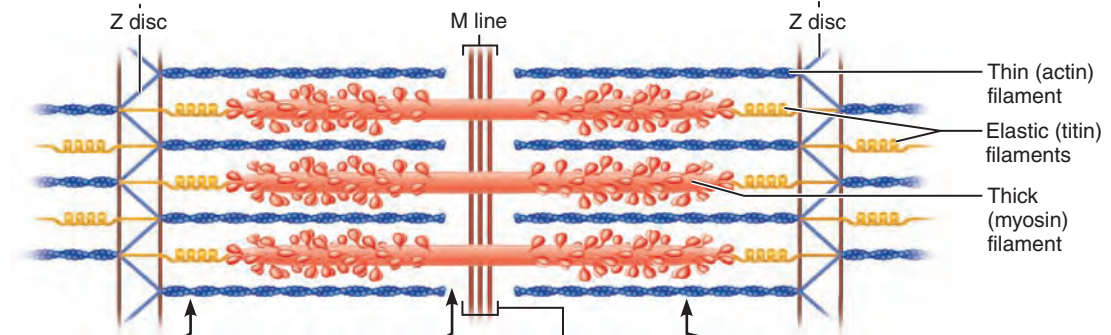
(b) Diagram of **part of a muscle fiber** showing the myofibrils. One **myofibril** extends from the cut end of the fiber.



(c) Small part of one **myofibril enlarged to show the myofilaments** responsible for the banding pattern. Each **sarcomere** extends from one Z disc to the next.



(d) **Enlargement of one sarcomere** (sectioned lengthwise). Notice the myosin heads on the thick filaments.



(e) **Cross-sectional view of a sarcomere** cut through in different locations.

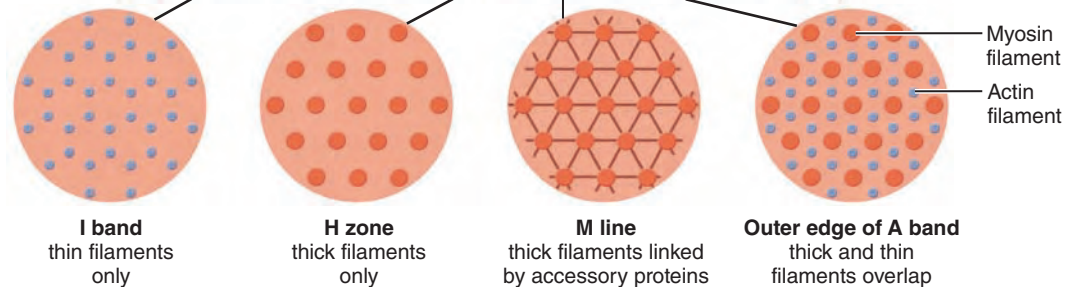


Figure 9.2 Microscopic anatomy of a skeletal muscle fiber. (For a related image, see *A Brief Atlas of the Human Body*, Plate 28.)

Myofibrils contain the contractile elements of skeletal muscle cells, the sarcomeres, which contain even smaller rodlike structures called *myofilaments*. Table 9.1 (bottom three rows; p. 283) summarizes these structures, which we discuss next.

Striations, Sarcomeres, and Myofilaments **Striations**, a repeating series of dark and light bands, are evident along the length of each myofibril. In an intact muscle fiber, the dark **A bands** and light **I bands** are nearly perfectly aligned, giving the cell its striated appearance.

As illustrated in Figure 9.2c:

- Each dark A band has a lighter region in its midsection called the **H zone** (H for *helle*; “bright”).
- Each H zone is bisected vertically by a dark line called the **M line** (M for middle) formed by molecules of the protein myomesin.
- Each light I band also has a midline interruption, a darker area called the **Z disc** (or Z line).
- The region of a myofibril between two successive Z discs is a **sarcomere** (sar’ko-mēr; literally, “muscle segment”). Averaging 2 μm long, a sarcomere is the smallest contractile unit of a muscle fiber—the *functional unit* of skeletal muscle. It contains an A band flanked by half an I band at each end. Within each myofibril, the sarcomeres align end to end like boxcars in a train.

If we examine the banding pattern of a myofibril at the molecular level, we see that it arises from orderly arrangement of even smaller structures within the sarcomeres. These smaller structures, the **myofilaments** or **filaments**, are the muscle equivalents of the actin- or myosin-containing microfilaments described in Chapter 3. As you will recall, the proteins actin and myosin play a role in motility and shape change in virtually every cell in the body. This property reaches its highest development in the contractile muscle fibers.

The central **thick filaments** containing myosin (red) extend the entire length of the A band (Figure 9.2c and d). They are connected in the middle of the sarcomere at the M line. The more lateral **thin filaments** containing actin (blue) extend across the I band and partway into the A band. The Z disc, a coin-shaped sheet composed largely of the protein alpha-actinin, anchors the thin filaments. We describe the third type of myofilament illustrated in Figure 9.2d, the *elastic filament*, in the next section. Intermediate (desmin) filaments (not illustrated) extend from the Z disc and connect each myofibril to the next throughout the width of the muscle cell.

Looking at the banding pattern more closely, we see that the H zone of the A band appears less dense because the thin filaments do not extend into this region. The M line in the center of the H zone is slightly darker because of the fine protein strands there that hold adjacent thick filaments together. The myofilaments are connected to the sarcolemma and held in alignment at the Z discs and the M lines.

A longitudinal view of the myofilaments (Figure 9.2d) is a bit misleading because it looks as if each thick (red) filament interdigitates with only four thin (blue) filaments. The cross section of a sarcomere on the far right in Figure 9.2e shows an

area where thick and thin filaments overlap. Notice that a hexagonal arrangement of six thin filaments surrounds each thick filament, and three thick filaments enclose each thin filament.

Molecular Composition of Myofilaments Muscle contraction depends on the myosin- and actin-containing myofilaments. As noted earlier, thick filaments (about 16 nm in diameter) are composed primarily of the protein **myosin**. Each myosin molecule consists of two heavy and four light polypeptide chains, and has a rodlike tail attached by a flexible hinge to two globular heads (Figure 9.3). The tail consists of two intertwined helical polypeptide heavy chains.

The globular heads, each associated with two light chains, are the “business end” of myosin. During contraction, they link the thick and thin filaments together, forming **cross bridges** (Figure 9.4 on p. 284), and swivel around their point of attachment. As we will explain shortly, these cross bridges act as motors to generate force.

Each thick filament contains about 300 myosin molecules bundled together, with their tails forming the central part of the thick filament and their heads facing outward at the end of each thick filament (Figure 9.3). As a result, the central portion of a thick filament (in the H zone) is smooth, but its ends are studded with a staggered array of myosin heads. The heads bear actin and ATP-binding sites and also have intrinsic ATPase activity that splits ATP to generate energy for muscle contraction.

The thin filaments (7–8 nm thick) are composed chiefly of the protein **actin** (blue in Figure 9.3). Actin has kidney-shaped polypeptide subunits, called *globular actin* or *G actin*, which bear the active sites to which the myosin heads attach during contraction. In the thin filaments, G actin subunits are polymerized into long actin filaments called *filamentous*, or *F actin*. Two intertwined actin filaments, resembling a twisted double strand of pearls, form the backbone of each thin filament (Figure 9.3).

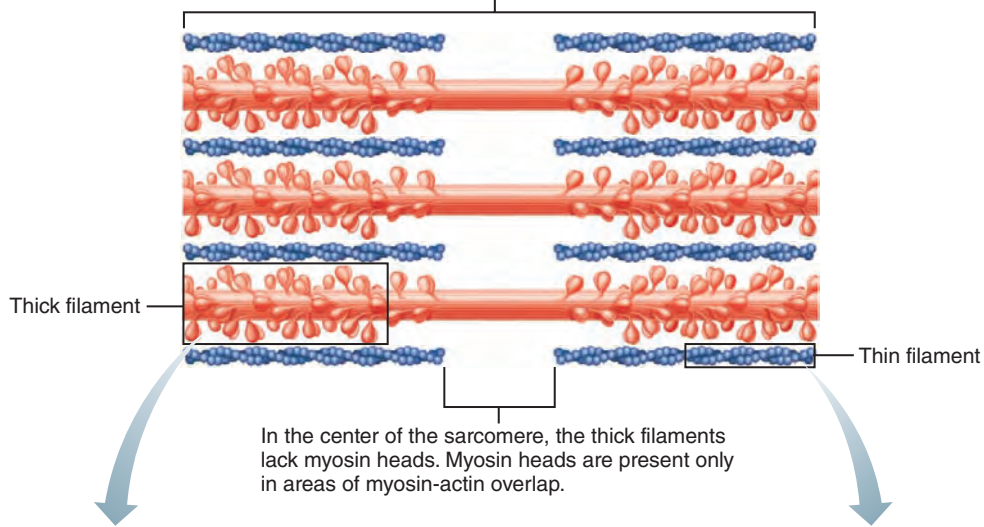
Thin filaments also contain several regulatory proteins.

- Polypeptide strands of **tropomyosin** (tro’po-mi’o-sin), a rod-shaped protein, spiral about the actin core and help stiffen and stabilize it. Successive tropomyosin molecules are arranged end to end along the actin filaments, and in a relaxed muscle fiber, they block myosin-binding sites on actin so that myosin heads on the thick filaments cannot bind to the thin filaments.
- **Troponin** (tro’po-nin), the other major protein in thin filaments, is a globular three-polypeptide complex (Figure 9.3). One of its polypeptides (TnI) is an inhibitory subunit that binds to actin. Another (TnT) binds to tropomyosin and helps position it on actin. The third (TnC) binds calcium ions.

Both troponin and tropomyosin help control the myosin-actin interactions involved in contraction. Several other proteins help form the structure of the myofibril.

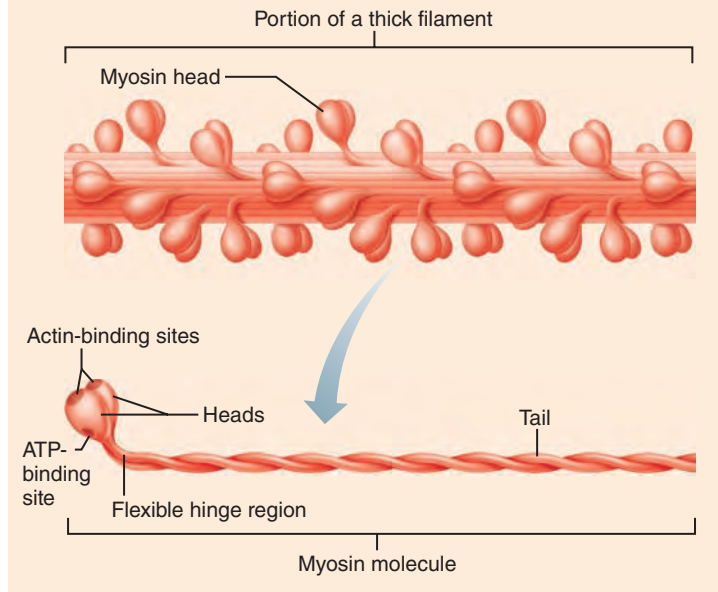
- The **elastic filament** we referred to earlier is composed of the giant protein **titin** (Figure 9.2d). Titin extends from the Z disc to the thick filament, and then runs within the thick filament (forming its core) to attach to the M line. It holds

Longitudinal section of filaments within one sarcomere of a myofibril



Thick filament

Each thick filament consists of many myosin molecules whose heads protrude at opposite ends of the filament.



Thin filament

A thin filament consists of two strands of actin subunits twisted into a helix plus two types of regulatory proteins (troponin and tropomyosin).

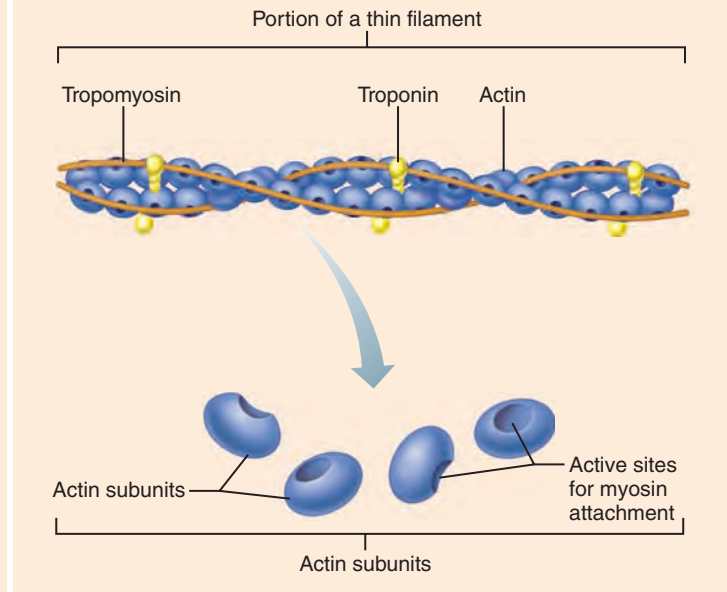


Figure 9.3 Composition of thick and thin filaments.

the thick filaments in place, thus maintaining the organization of the A band, and helps the muscle cell spring back into shape after stretching. (The part of the titin that spans the I bands is extensible, unfolding when the muscle stretches and recoiling when the tension is released.) Titin does not resist stretching in the ordinary range of extension, but it stiffens as it uncoils, helping the muscle resist excessive stretching, which might pull the sarcomeres apart.

- Another important structural protein is **dystrophin**, which links the thin filaments to the integral proteins of the

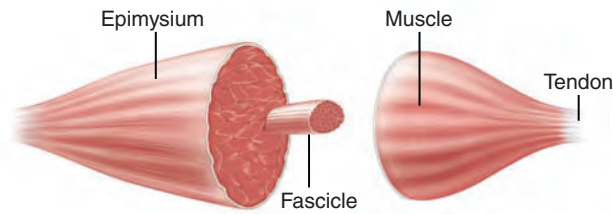
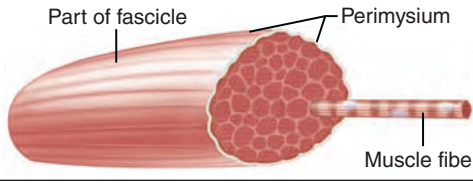
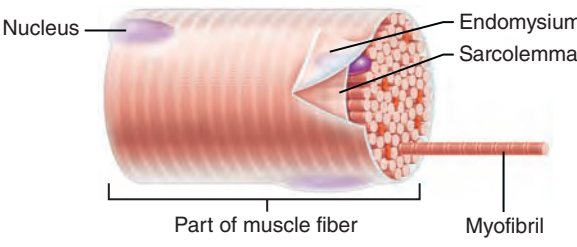
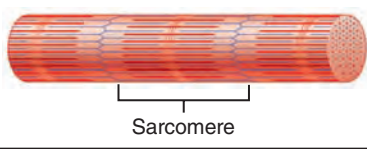
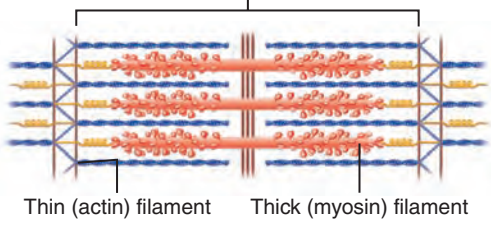
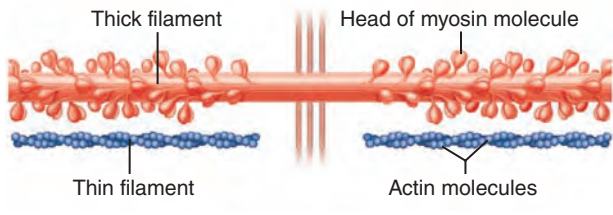
sarcolemma (which in turn are anchored to the extracellular matrix).

- Other proteins that bind filaments or sarcomeres together and maintain their alignment include *nebulin*, *myomesin*, and *C proteins*.

Sarcoplasmic Reticulum and T Tubules

Skeletal muscle fibers contain two sets of intracellular tubules that help regulate muscle contraction: (1) the sarcoplasmic reticulum and (2) T tubules.

Table 9.1 Structure and Organizational Levels of Skeletal Muscle

STRUCTURE AND ORGANIZATIONAL LEVEL	DESCRIPTION	CONNECTIVE TISSUE WRAPPINGS
<p>Muscle (organ)</p> 	<p>A muscle consists of hundreds to thousands of muscle cells, plus connective tissue wrappings, blood vessels, and nerve fibers.</p>	<p>Covered externally by the epimysium</p>
<p>Fascicle (a portion of the muscle)</p> 	<p>A fascicle is a discrete bundle of muscle cells, segregated from the rest of the muscle by a connective tissue sheath.</p>	<p>Surrounded by perimysium</p>
<p>Muscle Fiber (cell)</p> 	<p>A muscle fiber is an elongated multinucleate cell; it has a banded (striated) appearance.</p>	<p>Surrounded by endomysium</p>
<p>Myofibril or Fibril (complex organelle composed of bundles of myofilaments)</p> 	<p>Myofibrils are rodlike contractile elements that occupy most of the muscle cell volume. Composed of sarcomeres arranged end to end, they appear banded, and bands of adjacent myofibrils are aligned.</p>	<p>—</p>
<p>Sarcomere (a segment of a myofibril)</p> 	<p>A sarcomere is the contractile unit, composed of myofilaments made up of contractile proteins.</p>	<p>—</p>
<p>Myofilament or Filament (extended macromolecular structure)</p> 	<p>Contractile myofilaments are of two types—thick and thin. Thick filaments contain bundled myosin molecules; thin filaments contain actin molecules (plus other proteins). The sliding of the thin filaments past the thick filaments produces muscle shortening. Elastic filaments (not shown here) maintain the organization of the A band and provide elastic recoil when muscle contraction ends.</p>	<p>—</p>

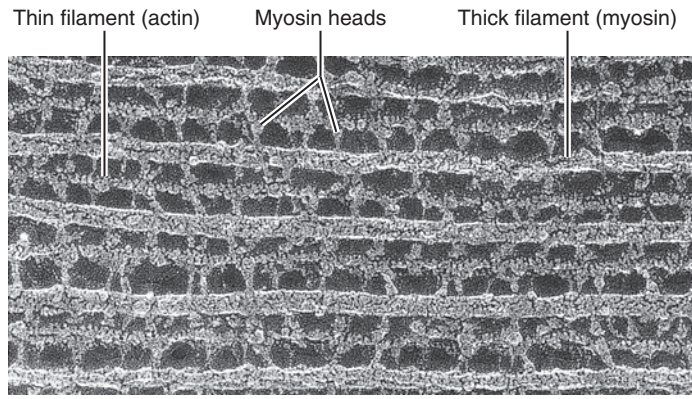


Figure 9.4 Myosin heads forming cross bridges that generate muscular contractile force. Part of a sarcomere is seen in a transmission electron micrograph (277,000 \times).

Sarcoplasmic Reticulum Shown in blue in **Figure 9.5**, the **sarcoplasmic reticulum (SR)** is an elaborate smooth endoplasmic reticulum. Its interconnecting tubules surround each myofibril the way the sleeve of a loosely crocheted sweater surrounds your arm.

Most SR tubules run longitudinally along the myofibril, communicating with each other at the H zone. Others called **terminal cisterns** (“end sacs”) form larger, perpendicular cross channels at the A band–I band junctions and they always occur in pairs. Closely associated with the SR are large numbers of

mitochondria and glycogen granules, both involved in producing the energy used during contraction.

The SR regulates intracellular levels of ionic calcium. It stores calcium and releases it on demand when the muscle fiber is stimulated to contract. As you will see, calcium provides the final “go” signal for contraction.

T Tubules At each A band–I band junction, the sarcolemma of the muscle cell protrudes deep into the cell interior, forming an elongated tube called the **T tubule** (T for “transverse”). The T tubules, shown in gray in **Figure 9.5**, tremendously increase the muscle fiber’s surface area. Possibly the result of fusing tubelike caveolae (inpocketings of the sarcolemma), the *lumen* (cavity) of the T tubule is continuous with the extracellular space.

Along its length, each T tubule runs between the paired terminal cisterns of the SR, forming **triads**, successive groupings of the three membranous structures (terminal cistern, T tubule, and terminal cistern). As they pass from one myofibril to the next, the T tubules also encircle each sarcomere.

Muscle contraction is ultimately controlled by nerve-initiated electrical impulses that travel along the sarcolemma. Because T tubules are continuations of the sarcolemma, they conduct impulses to the deepest regions of the muscle cell and every sarcomere. These impulses signal for the release of calcium from the adjacent terminal cisterns. Think of the T tubules as a rapid telegraph system that ensures that every myofibril in the muscle fiber contracts at virtually the same time.

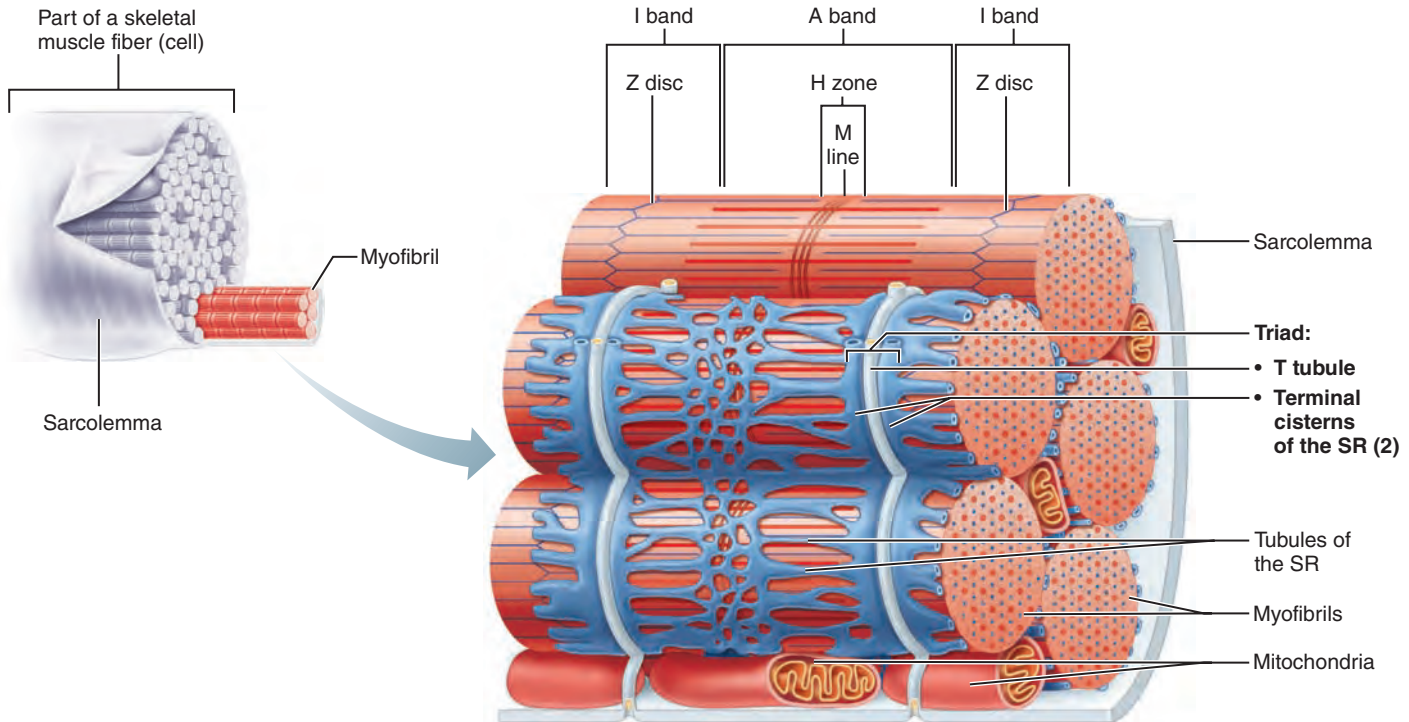


Figure 9.5 Relationship of the sarcoplasmic reticulum and T tubules to myofibrils of skeletal muscle. The tubules of the SR (blue) fuse to form a net of communicating channels at the level

of the H zone and the saclike terminal cisterns abutting the A–I junctions. The T tubules (gray) are inward invaginations of the sarcolemma that run deep into the cell between the terminal cisterns. (See detailed

view in **Figure 9.11**, pp. 290–291.) Sites of close contact of these three elements (terminal cistern, T tubule, and terminal cistern) are called triads.

Triad Relationships The roles of the T tubules and SR in providing signals for contraction are tightly linked. At the triads, where these organelles come into closest contact, integral proteins (some from the T tubule and others from the SR) protrude into the intermembrane spaces. The protruding integral proteins of the T tubule act as voltage sensors. Those of the SR form gated channels through which the terminal cisterns release Ca^{2+} . We will return to their interaction shortly.

Sliding Filament Model of Contraction

We almost always think “shortening” when we hear the word **contraction**, but to physiologists the term refers only to the activation of myosin’s cross bridges, which are the force-generating sites. Shortening occurs if and when the cross bridges generate enough tension on the thin filaments to exceed the forces that oppose shortening. Contraction ends when the cross bridges become inactive, the tension declines, and then the muscle fiber relaxes.

In a relaxed muscle fiber, the thin and thick filaments overlap only at the ends of the A band (Figure 9.6 ①). The **sliding filament model of contraction** states that during contraction the thin filaments slide past the thick ones so that the actin and myosin filaments overlap to a greater degree:

- When the nervous system stimulates muscle fibers, the myosin heads on the thick filaments latch onto myosin-binding sites on actin in the thin filaments, and the sliding begins.
- These cross bridge attachments form and break several times during a contraction, acting like tiny ratchets to generate tension and propel the thin filaments toward the center of the sarcomere.
- As this event occurs simultaneously in sarcomeres throughout the cell, the muscle cell shortens.
- Notice that as the thin filaments slide centrally, the Z discs to which they attach are pulled *toward* the M line (Figure 9.6 ②). Overall, as a muscle cell shortens: (1) the I bands shorten, (2) the distance between successive Z discs shortens, (3) the H zones disappear, and (4) the contiguous A bands move closer together but their length does not change.

✓ Check Your Understanding

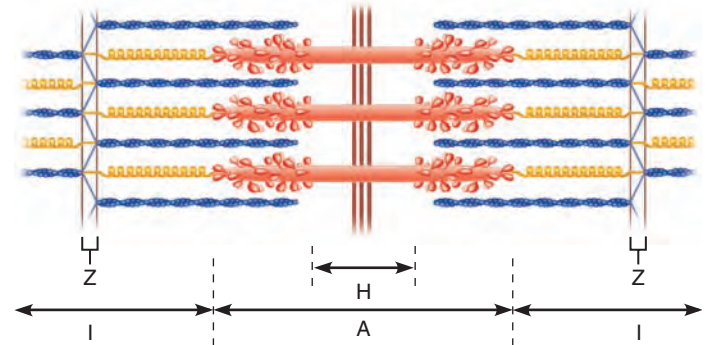
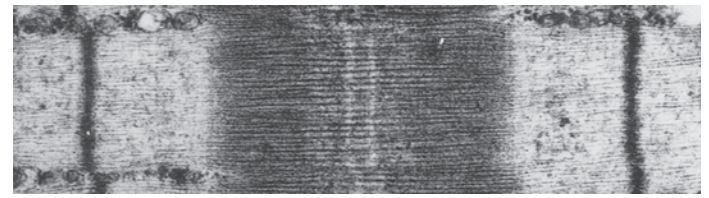
3. How does the term epimysium relate to the role and position of this connective tissue sheath?
4. Which myofilaments have binding sites for calcium? What specific molecule binds calcium?
5. Which region or organelle—cytosol, mitochondrion, or SR—contains the highest concentration of calcium ions in a resting muscle fiber? Which structure provides the ATP needed for muscle activity?

For answers, see Appendix H.

Physiology of Skeletal Muscle Fibers

- ✓ Explain how muscle fibers are stimulated to contract by describing events that occur at the neuromuscular junction.
- ✓ Describe how an action potential is generated.

① Fully relaxed sarcomere of a muscle fiber



② Fully contracted sarcomere of a muscle fiber

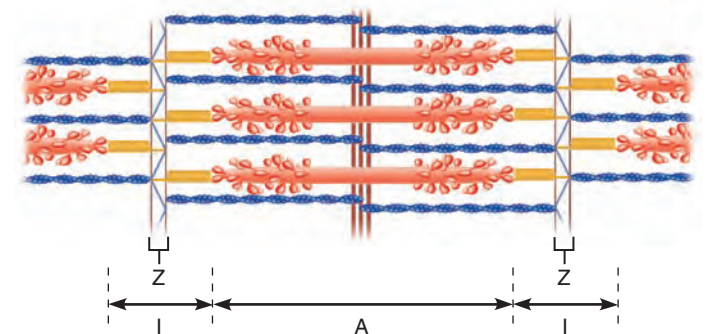
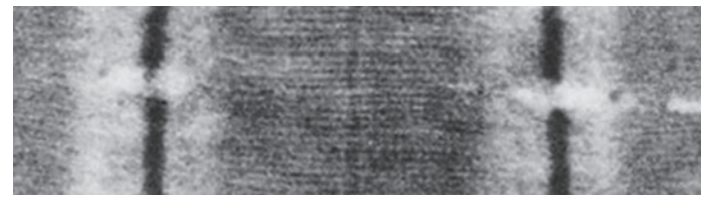


Figure 9.6 Sliding filament model of contraction. The numbers indicate events in a ① relaxed and a ② fully contracted sarcomere. At full contraction, the Z discs about the thick filaments and the thin filaments overlap each other. The photomicrographs (top view in each case) show enlargements of 33,000 \times .

- ✓ Follow the events of excitation-contraction coupling that lead to cross bridge activity.

The sliding filament model tells us how a muscle fiber contracts, but what induces it to contract in the first place? For a skeletal muscle fiber to contract:

1. The fiber must be activated, that is, stimulated by a nerve ending so that a change in membrane potential occurs.
2. Next, it must generate an electrical current, called an **action potential**, in its sarcolemma.

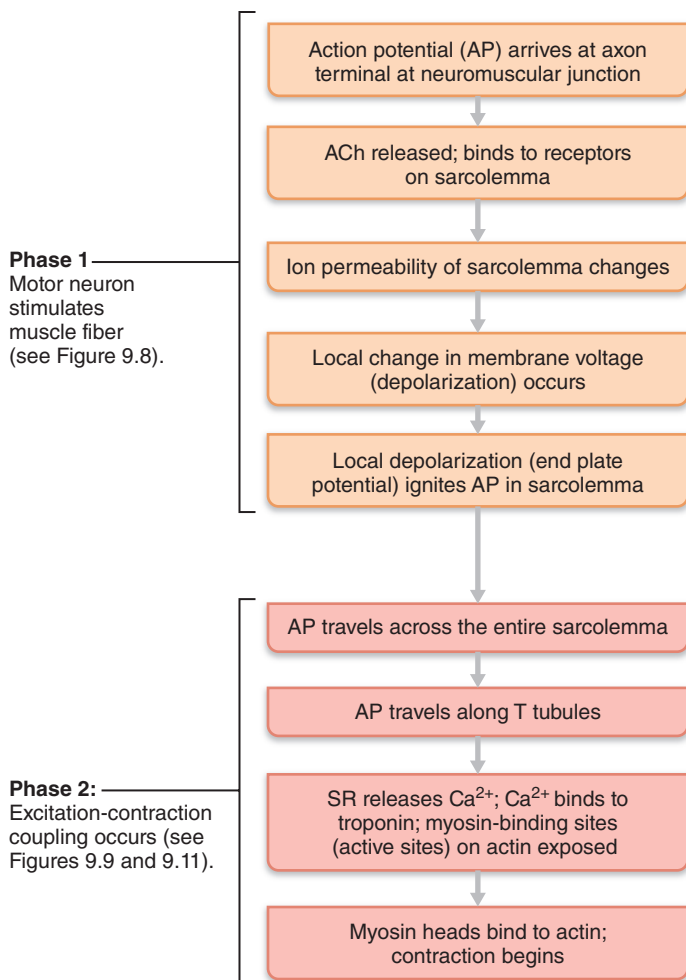


Figure 9.7 The phases leading to muscle fiber contraction.

- The action potential is automatically propagated along the sarcolemma.
- Then, intracellular calcium ion levels must rise briefly, providing the final trigger for contraction.

Steps 1 and 2, activation, occur at the neuromuscular junction and set the stage for the events that follow. Steps 3 and 4, which link the electrical signal to contraction, are called excitation-contraction coupling. **Figure 9.7** summarizes this series of events into two major phases, which we consider in detail below.

The Nerve Stimulus and Events at the Neuromuscular Junction

The nerve cells that activate skeletal muscle fibers are called *somatic motor neurons*, or *motor neurons of the somatic (voluntary) nervous system*. These motor neurons “reside” in the brain or spinal cord, but their long threadlike extensions called axons travel, bundled within nerves, to the muscle cells they serve.

The axon of each motor neuron divides profusely as it enters the muscle. Each axon ending gives off several short, curling branches that collectively form an elliptical **neuromuscular junction**, or **end plate**, with a single muscle fiber.

As a rule, each muscle fiber has only one neuromuscular junction, located approximately midway along its length. The axon terminal and the muscle fiber are exceedingly close (50–80 nm apart), but they remain separated by a space, the **synaptic cleft** (Figure 9.8), which is filled with a gel-like extracellular substance rich in glycoproteins and collagen fibers.

Within the moundlike axon terminal are **synaptic vesicles**, small membranous sacs containing the neurotransmitter **acetylcholine** (as’ē-til-ko’lën), or **ACh**. The trough-like part of the muscle fiber’s sarcolemma that helps form the neuromuscular junction is highly folded. These **junctional folds** provide a large surface area for the millions of **ACh receptors** located there. Hence, the neuromuscular junction includes the axon terminals, the synaptic cleft, and the junctional folds of the sarcolemma.

How does a motor neuron stimulate a skeletal muscle fiber? The simplest explanation is:

- When a nerve impulse reaches the end of an axon, the axon terminal releases ACh into the synaptic cleft.
- ACh diffuses across the cleft and attaches to ACh receptors on the sarcolemma of the muscle fiber.
- ACh binding triggers electrical events that ultimately generate an action potential.

Focus on Events at the Neuromuscular Junction (Figure 9.8) covers this process step by step. Study this figure before continuing.

After ACh binds to the ACh receptors, its effects are quickly terminated by **acetylcholinesterase** (as’ē-til-ko’lin-es’ter-ās), an enzyme located in the synaptic cleft. Acetylcholinesterase breaks down ACh to its building blocks, acetic acid and choline. This removal of ACh prevents continued (and most likely undesirable) muscle fiber contraction in the absence of additional nervous system stimulation.

Homeostatic Imbalance 9.1

Many toxins, drugs, and diseases interfere with events at the neuromuscular junction. For example, *myasthenia gravis* (*asthen* = weakness; *gravi* = heavy), a disease characterized by drooping upper eyelids, difficulty swallowing and talking, and generalized muscle weakness, involves a shortage of ACh receptors. Serum analysis reveals antibodies to ACh receptors, suggesting that myasthenia gravis is an autoimmune disease. Although normal numbers of receptors are initially present, they appear to be destroyed as the disease progresses. +

Generation of an Action Potential Across the Sarcolemma

Like the plasma membranes of all cells, a resting sarcolemma is *polarized*. That is, a voltmeter would show there is a potential difference (voltage) across the membrane and the inside is negative relative to the outer membrane face. (Chapter 3 describes the resting membrane potential.)

An action potential (AP) is the result of a predictable sequence of electrical changes. Once initiated, they occur along

Figure 9.8 When a nerve impulse reaches a neuromuscular junction, acetylcholine (ACh) is released. Upon binding to sarcolemma receptors, ACh causes a change in sarcolemma permeability leading to a change in membrane potential.

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1 Action potential arrives at axon terminal of motor neuron.

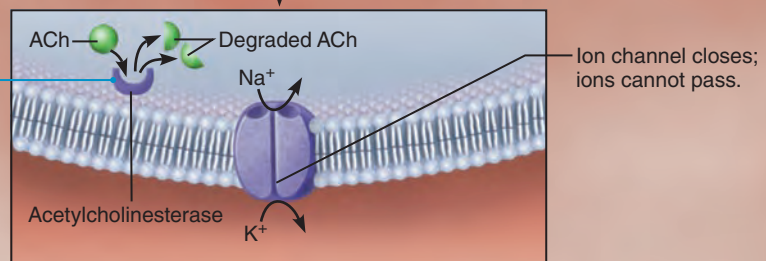
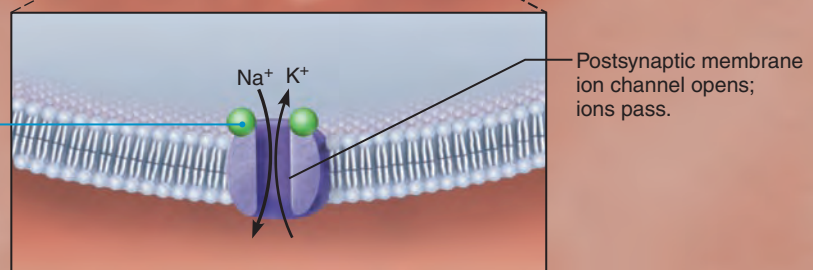
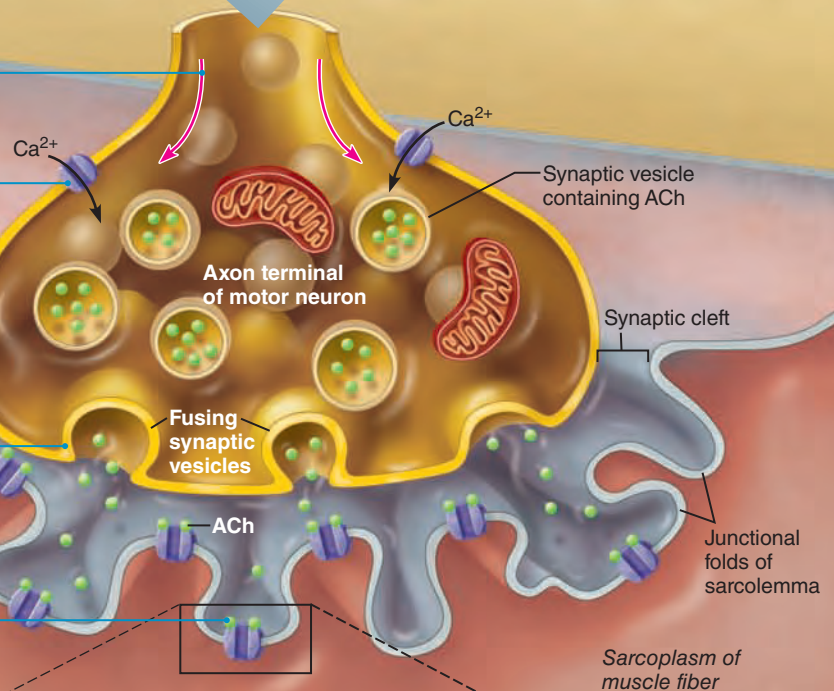
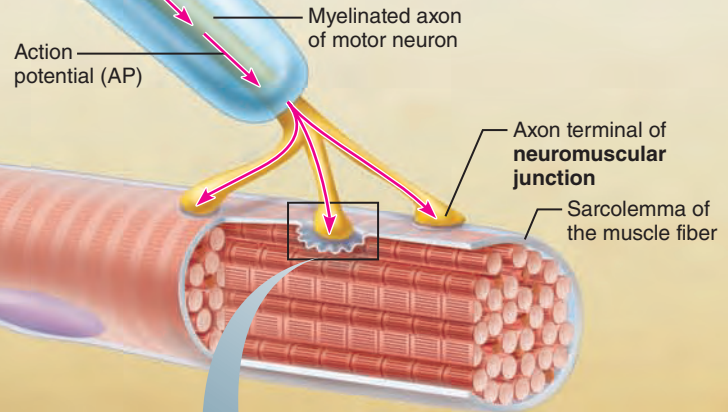
2 Voltage-gated Ca^{2+} channels open. Ca^{2+} enters the axon terminal moving down its electrochemical gradient.

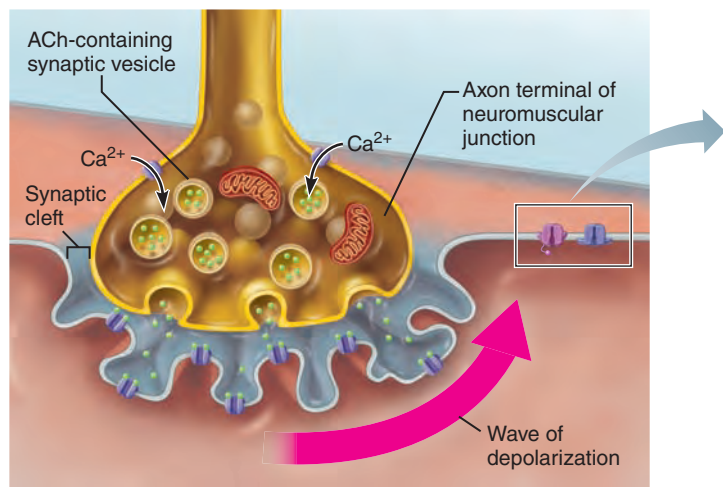
3 Ca^{2+} entry causes ACh (a neurotransmitter) to be released by exocytosis.

4 ACh diffuses across the synaptic cleft and binds to its receptors on the sarcolemma.

5 ACh binding opens ion channels in the receptors that allow simultaneous passage of Na^+ into the muscle fiber and K^+ out of the muscle fiber. More Na^+ ions enter than K^+ ions exit, which produces a local change in the membrane potential called the end plate potential.

6 ACh effects are terminated by its breakdown in the synaptic cleft by acetylcholinesterase and diffusion away from the junction.



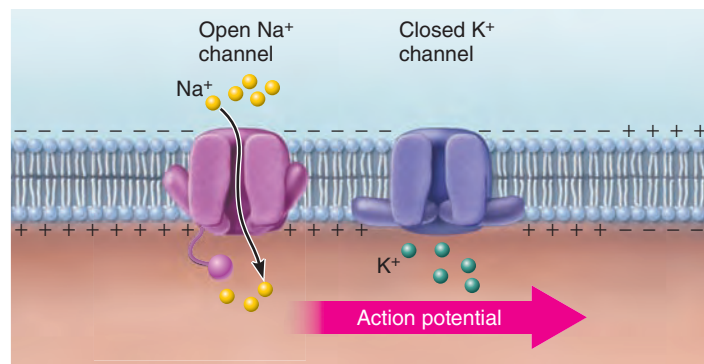


① An end plate potential is generated at the neuromuscular junction (see Figure 9.8).

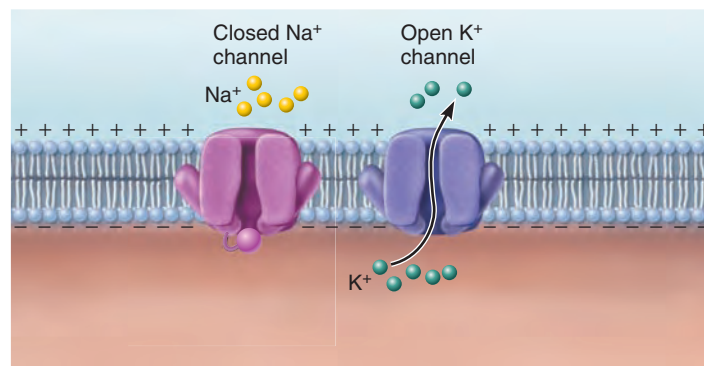
Figure 9.9 Summary of events in the generation and propagation of an action potential in a skeletal muscle fiber.

the entire surface of the sarcolemma. Essentially three steps are involved (**Figure 9.9**):

- ① **Generation of an end plate potential.** Binding of ACh molecules to ACh receptors at the neuromuscular junction opens *chemically (ligand) gated ion channels* that allow Na⁺ and K⁺ to pass (also see Figure 9.8). Because the driving force for Na⁺ is greater than that for K⁺, more Na⁺ diffuses in than K⁺ diffuses out. A transient change in membrane potential occurs as the interior of the sarcolemma becomes less negative, an event called depolarization. Initially, depolarization is a local event called an **end plate potential**.
- ② **Depolarization: Generation and propagation of an action potential.** The end plate potential (local depolarization at the neuromuscular junction) ignites an action potential by spreading to adjacent membrane areas and opening voltage-gated sodium channels there. Na⁺ enters, following its electrochemical gradient, and once a certain



- ② **Depolarization: Generating and propagating an action potential (AP).** The local depolarization current spreads to adjacent areas of the sarcolemma. This opens voltage-gated sodium channels there, so Na⁺ enters following its electrochemical gradient and initiates the AP. The AP is propagated as its local depolarization wave spreads to adjacent areas of the sarcolemma, opening voltage-gated channels there. Again Na⁺ diffuses into the cell following its electrochemical gradient.



- ③ **Repolarization: Restoring the sarcolemma to its initial polarized state (negative inside, positive outside).** Repolarization occurs as Na⁺ channels close (inactivate) and voltage-gated K⁺ channels open. Because K⁺ concentration is substantially higher inside the cell than in the extracellular fluid, K⁺ diffuses rapidly out of the muscle fiber.

membrane voltage, referred to as *threshold*, is reached, an action potential is generated (initiated).

The action potential *propagates* (moves along the length of the sarcolemma) in all directions from the neuromuscular junction, just as ripples move away from a pebble dropped into a stream. As it propagates, the local depolarization wave of the AP spreads to adjacent areas of the sarcolemma and opens voltage-gated sodium channels there. Again, Na⁺, normally restricted from entering, diffuses into the cell following its electrochemical gradient.

- ③ **Repolarization: Restoring the sarcolemma to its initial polarized state.** The repolarization wave, like the depolarization wave, is a consequence of changes in membrane permeability. In this case, Na⁺ channels close and voltage-gated K⁺ channels open. Since the potassium ion concentration is substantially higher inside the cell than in the extracellular fluid, K⁺ diffuses rapidly out of the muscle

fiber, restoring negatively charged conditions inside (also see **Figure 9.10**).

During repolarization, a muscle fiber is said to be in a **refractory period**, because the cell cannot be stimulated again until repolarization is complete. Note that repolarization restores only the *electrical conditions* of the resting (polarized) state. The ATP-dependent Na^+ - K^+ pump restores the *ionic conditions* of the resting state, but hundreds of action potentials can occur before ionic imbalances interfere with contractile activity.

Once initiated, the action potential is unstoppable. It ultimately results in contraction of the muscle fiber. Although the action potential itself lasts only a few milliseconds (ms), the contraction phase of a muscle fiber may persist for 100 ms or more and far outlasts the electrical event that triggers it.

Excitation-Contraction Coupling

Excitation-contraction (E-C) coupling is the sequence of events by which transmission of an action potential along the sarcolemma causes myofilaments to slide. The action potential is brief and ends well before any signs of contraction are obvious.

As you will see, the electrical signal does not act directly on the myofilaments. Instead, it causes the rise in intracellular levels of calcium ions, which allows the filaments to slide.

Focus on Excitation-Contraction Coupling (Figure 9.11) on pp. 290–291 illustrates the steps in this process. This Focus feature also reveals how the integral proteins of the T tubules and terminal cisterns in the triads interact to provide the Ca^{2+} necessary for contraction to occur. Make sure you understand this material before continuing.

Summary: Channels Involved in Initiating Muscle Contraction

So let's summarize what has to happen to excite a muscle cell, starting from the nerve ending. Essentially this process activates four sets of ion channels:

1. The process begins when the nerve impulse reaches the axon terminal and opens voltage-gated calcium channels in the axonal membrane. Calcium entry triggers release of ACh into the synaptic cleft.
2. Released ACh binds to ACh receptors in the sarcolemma, opening chemically gated Na^+ - K^+ channels. Greater influx of Na^+ causes a local voltage change (the end plate potential).
3. Local depolarization opens voltage-gated sodium channels in the neighboring region of the sarcolemma. This allows more sodium to enter, which further depolarizes the sarcolemma, generating and propagating an AP.
4. Transmission of the AP along the T tubules changes the shape of voltage-sensitive proteins in the T tubules, which in turn stimulate SR calcium release channels to release Ca^{2+} into the cytosol.

Muscle Fiber Contraction: Cross Bridge Cycling

As we have noted, cross bridge formation (attachment of myosin heads to actin) requires Ca^{2+} . Let's look more closely at how calcium ions promote muscle cell contraction.

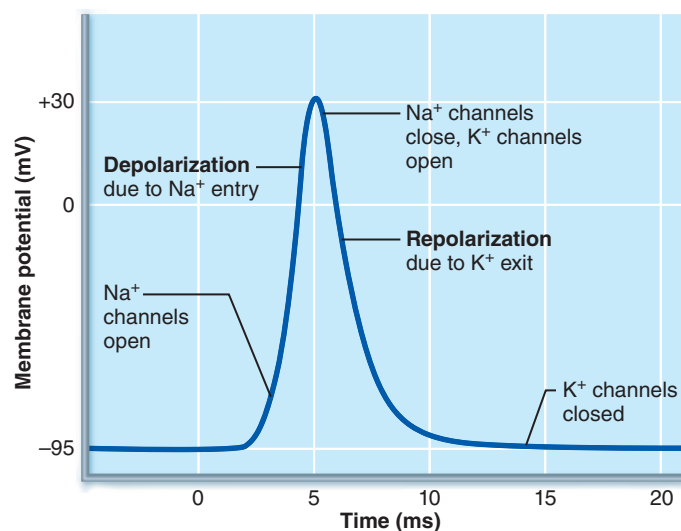


Figure 9.10 Action potential tracing indicates changes in Na^+ and K^+ ion channels.

When intracellular calcium levels are low, the muscle cell is relaxed, and tropomyosin molecules physically block the active (myosin-binding) sites on actin. As Ca^{2+} levels rise, the ions bind to regulatory sites on troponin. To activate its group of seven actins, a troponin must bind two calcium ions, change shape, and then roll tropomyosin into the groove of the actin helix, away from the myosin-binding sites. In short, the tropomyosin “blockade” is removed when sufficient calcium is present. Once binding sites on actin are exposed, the events of the cross bridge cycle occur in rapid succession, as depicted in *Focus on the Cross Bridge Cycle (Figure 9.12)* on p. 292.

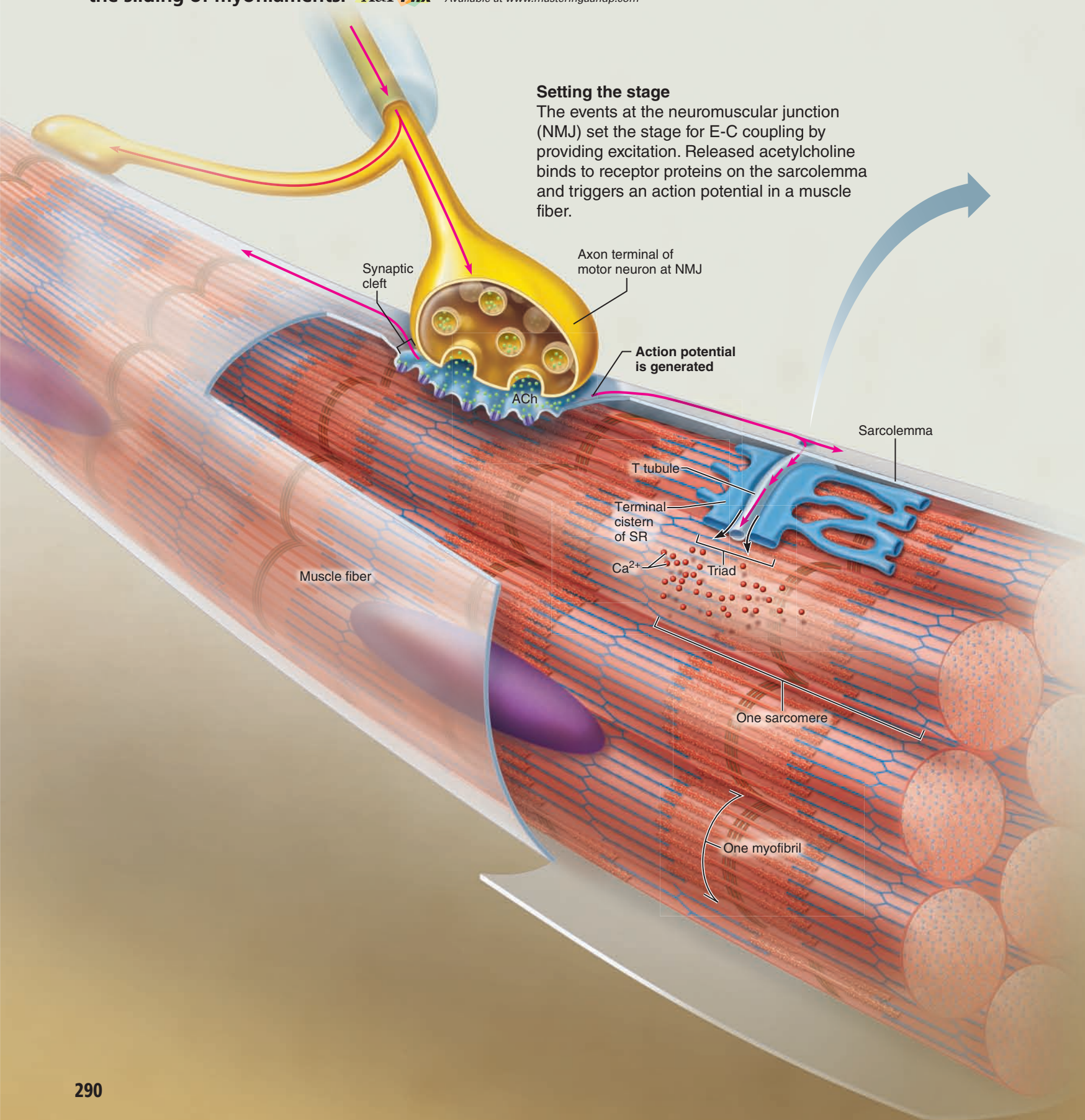
The thin filaments continue to slide as long as the calcium signal and adequate ATP are present. When nerve impulses arrive rapidly, intracellular Ca^{2+} levels soar due to successive “puffs” or rounds of Ca^{2+} released from the SR. In such cases, the muscle cells do not completely relax between successive stimuli and contraction is stronger and more sustained (within limits) until nervous stimulation ceases.

As the Ca^{2+} pumps of the SR reclaim calcium ions from the cytosol and troponin again changes shape, tropomyosin again blocks actin's myosin-binding sites. The contraction ends, and the muscle fiber relaxes.

When the cycle is ready to start again, the myosin head is in its upright high-energy configuration (see step ④ in Focus Figure 9.12), ready to take another “step” and attach to an actin site farther along the thin filament. This “walking” of the myosin heads along the adjacent thin filaments during muscle shortening is much like a centipede's gait. The thin filaments cannot slide backward as the cycle repeats again and again because some myosin heads (“legs”) are always in contact with actin (the “ground”). Contracting muscles routinely shorten by 30–35% of their total resting length, so each myosin cross bridge attaches and detaches many times during a single contraction. It is likely that only half of the myosin heads of a thick filament are pulling at the same instant. The others are randomly seeking their next binding site.

(Text continues on p. 293.)

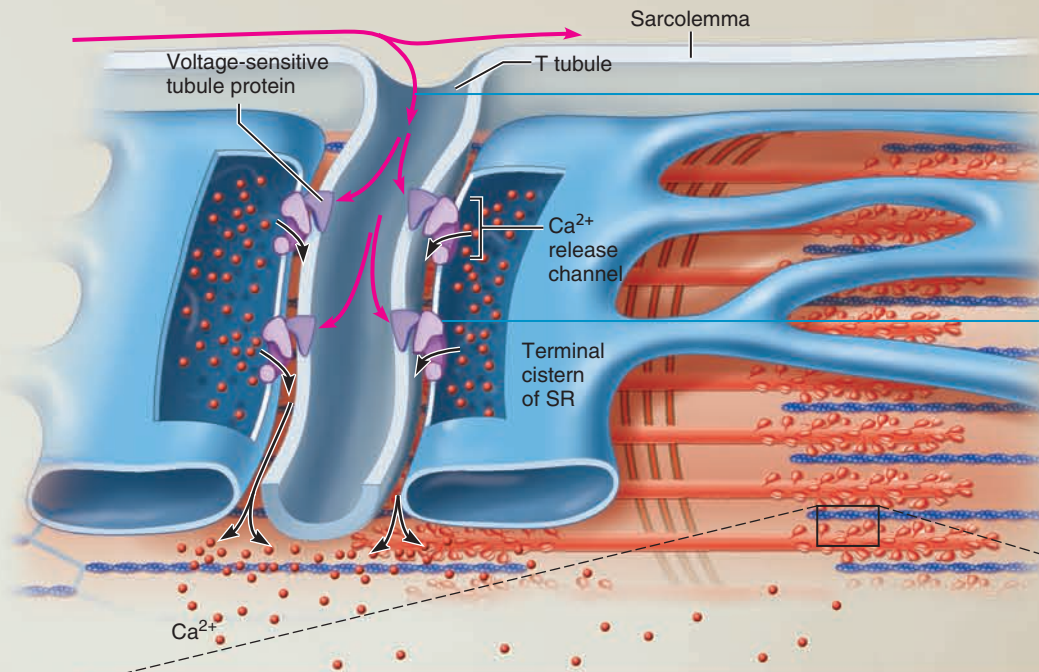
Figure 9.11 Excitation-contraction (E-C) coupling is the sequence of events by which transmission of an action potential along the sarcolemma leads to the sliding of myofilaments. *A&P Flix* Available at www.masteringaandp.com



Setting the stage

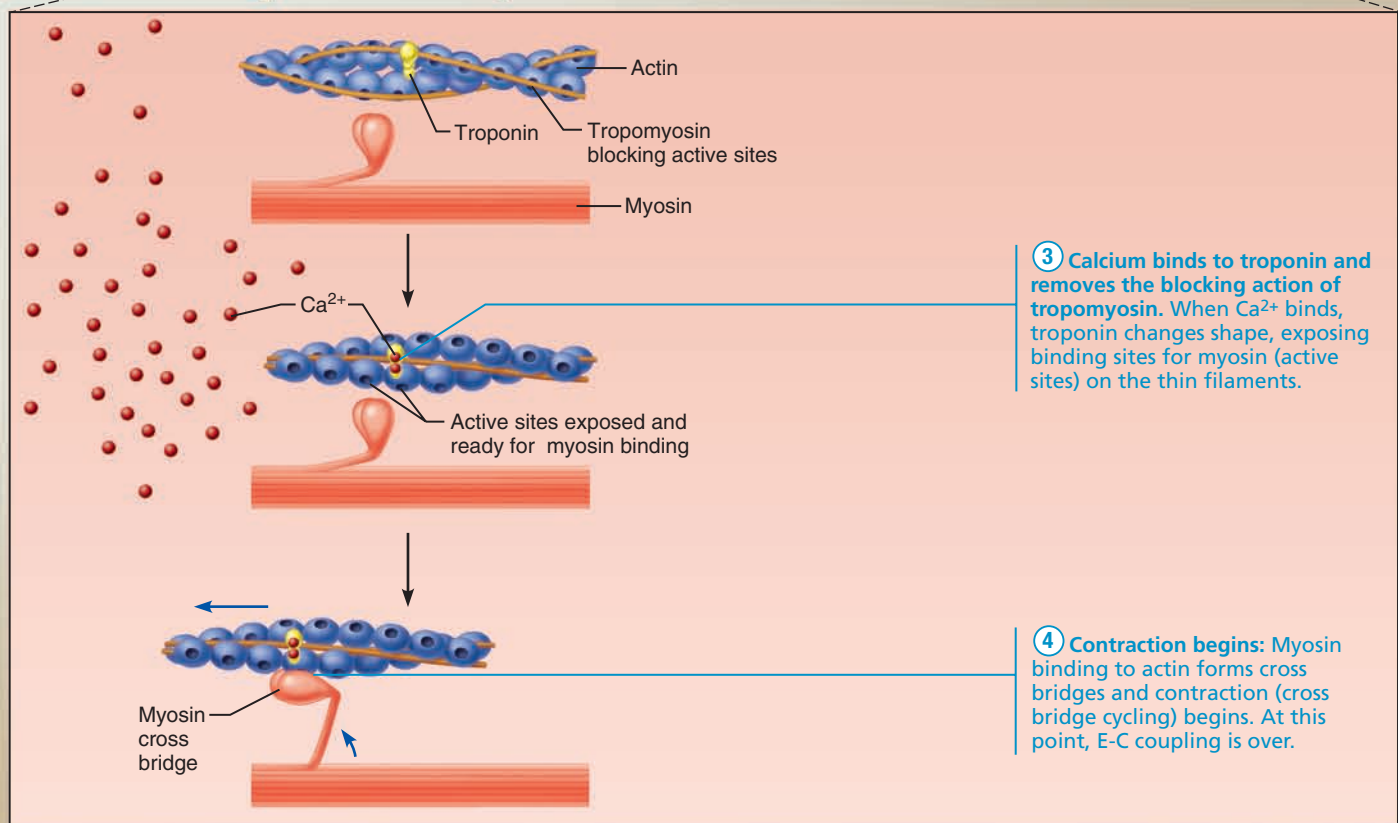
The events at the neuromuscular junction (NMJ) set the stage for E-C coupling by providing excitation. Released acetylcholine binds to receptor proteins on the sarcolemma and triggers an action potential in a muscle fiber.

Steps in E-C Coupling:



① The action potential (AP) propagates along the sarcolemma and down the T tubules.

② Calcium ions are released. Transmission of the AP along the T tubules of the triads causes the voltage-sensitive tubule proteins to change shape. This shape change opens the Ca²⁺ release channels in the terminal cisterns of the sarcoplasmic reticulum (SR), allowing Ca²⁺ to flow into the cytosol.



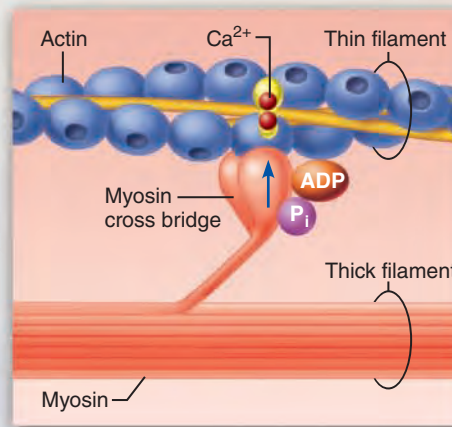
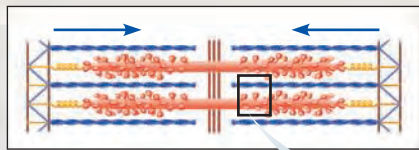
③ Calcium binds to troponin and removes the blocking action of tropomyosin. When Ca²⁺ binds, troponin changes shape, exposing binding sites for myosin (active sites) on the thin filaments.

④ Contraction begins: Myosin binding to actin forms cross bridges and contraction (cross bridge cycling) begins. At this point, E-C coupling is over.

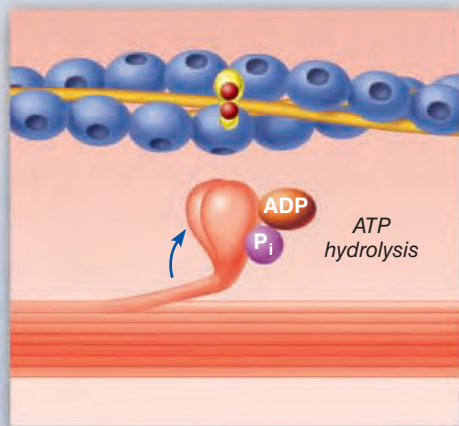
The aftermath

When the muscle AP ceases, the voltage-sensitive tubule proteins return to their original shape, closing the Ca²⁺ release channels of the SR. Ca²⁺ levels in the sarcoplasm fall as Ca²⁺ is continually pumped back into the SR by active transport. Without Ca²⁺, the blocking action of tropomyosin is restored, myosin-actin interaction is inhibited, and relaxation occurs. Each time an AP arrives at the neuromuscular junction, the sequence of E-C coupling is repeated.

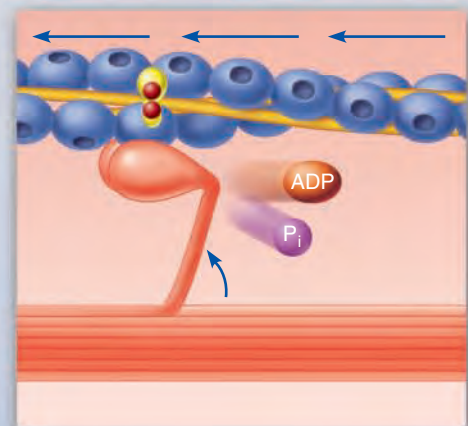
Figure 9.12 The cross bridge cycle is the series of events during which myosin heads pull thin filaments toward the center of the sarcomere. *A&P Flix* Available at www.masteringaandp.com



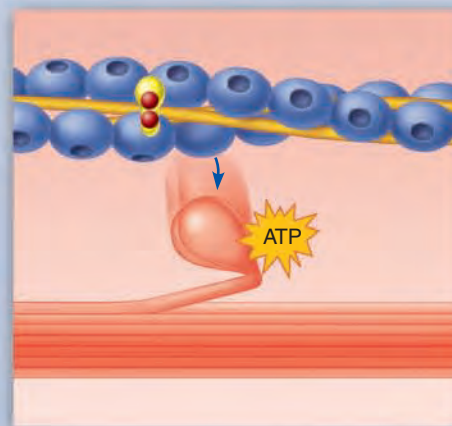
1 Cross bridge formation. Energized myosin head attaches to an actin myofilament, forming a cross bridge.



4 Cocking of the myosin head. As ATP is hydrolyzed to ADP and P_i , the myosin head returns to its prestroke high-energy, or "cocked," position.*



2 The power (working) stroke. ADP and P_i are released and the myosin head pivots and bends, changing to its bent low-energy state. As a result it pulls the actin filament toward the M line.



3 Cross bridge detachment. After ATP attaches to myosin, the link between myosin and actin weakens, and the myosin head detaches (the cross bridge "breaks").

In the absence of ATP, myosin heads will not detach, causing rigor mortis.

*This cycle will continue as long as ATP is available and Ca^{2+} is bound to troponin.

Except for the brief period following muscle cell excitation, calcium ion concentrations in the cytosol are kept almost undetectably low. There is a reason for this: Sustained high calcium activates apoptosis, leading to cell death.

Homeostatic Imbalance 9.2




Rigor mortis (death rigor) illustrates the fact that cross bridge detachment is ATP driven. Most muscles begin to stiffen 3 to 4 hours after death. Peak rigidity occurs at 12 hours and then gradually dissipates over the next 48 to 60 hours. Dying cells are unable to exclude calcium (which is in higher concentration in the extracellular fluid), and the calcium influx into muscle cells promotes formation of myosin cross bridges. Shortly after breathing stops, ATP synthesis ceases, but ATP continues to be consumed and cross bridge detachment is impossible. Actin and myosin become irreversibly cross-linked, producing the stiffness of rigor mortis, which gradually disappears as muscle proteins break down after death. +

Check Your Understanding

6. What are the three structural components of a neuromuscular junction?
7. What is the final trigger for contraction? What is the initial trigger?
8. What prevents the filaments from sliding back to their original position each time a myosin cross bridge detaches from actin?
9. What would happen if a muscle fiber suddenly ran out of ATP when sarcomeres had only partially contracted?

For answers, see Appendix H.

Contraction of a Skeletal Muscle

-  Define motor unit and muscle twitch, and describe the events occurring during the three phases of a muscle twitch.
-  Explain how smooth, graded contractions of a skeletal muscle are produced.
-  Differentiate between isometric and isotonic contractions.

In its relaxed state, a muscle is soft and unimpressive, not what you would expect of a prime mover of the body. However, within a few milliseconds, it can contract to become a hard elastic structure with dynamic characteristics that intrigue not only biologists but engineers and physicists as well.

Before we consider muscle contraction on the organ level, let's note a few principles of muscle mechanics.

- The principles governing contraction of a single muscle fiber and of a skeletal muscle consisting of a large number of fibers are pretty much the same.
- The force exerted by a contracting muscle on an object is called **muscle tension**. The opposing force exerted on the muscle by the weight of the object to be moved is called the **load**.
- A contracting muscle does not always shorten and move the load. If muscle tension develops but the load is not moved, the contraction is called *isometric* (“same measure”)—think

of trying to lift a 2000-lb car. If the muscle tension developed overcomes the load and muscle shortening occurs, the contraction is *isotonic* (“same tension”), as when you lift a 5-lb sack of sugar. We will describe isometric and isotonic contractions in detail, but for now the important thing to remember when reading the accompanying graphs is this: *Increasing muscle tension* is measured for isometric contractions, whereas the *amount of muscle shortening* (distance in millimeters) is measured for isotonic contractions.

- A skeletal muscle contracts with varying force and for different periods of time in response to stimuli of varying frequencies and intensities. To understand how this occurs, we must look at the nerve-muscle functional unit called a *motor unit*. This is our next topic.

The Motor Unit

Each muscle is served by at least one *motor nerve*, and each motor nerve contains axons (fibrous extensions) of up to hundreds of motor neurons. As an axon enters a muscle, it branches into a number of terminals, each of which forms a neuromuscular junction with a single muscle fiber. A **motor unit** consists of one motor neuron and all the muscle fibers it innervates, or supplies (**Figure 9.13**). When a motor neuron fires (transmits an action potential), all the muscle fibers it innervates contract.

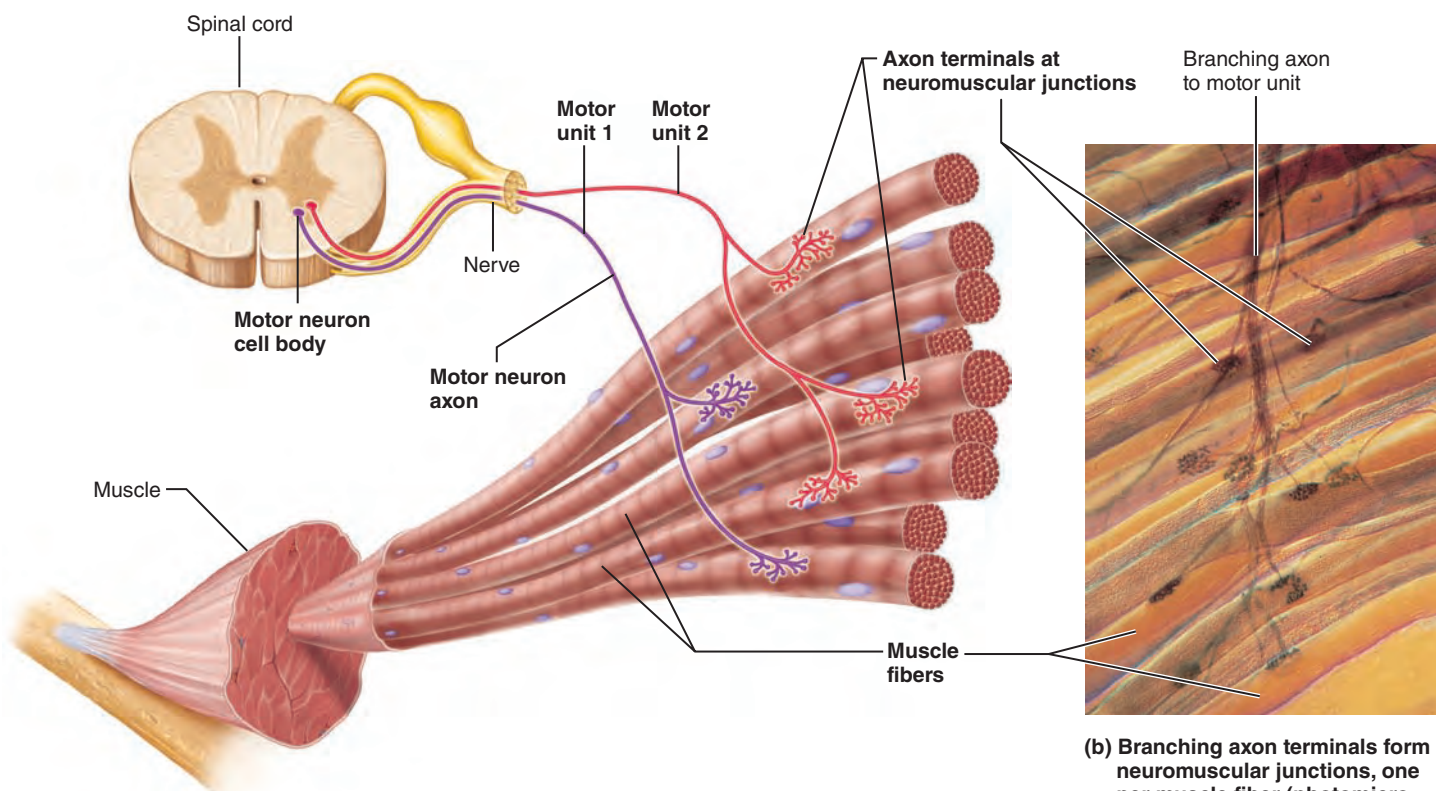
The number of muscle fibers per motor unit may be as high as several hundred or as few as four. Muscles that exert fine control (such as those controlling the fingers and eyes) have small motor units. By contrast, large, weight-bearing muscles, whose movements are less precise (such as the hip muscles), have large motor units. The muscle fibers in a single motor unit are not clustered together but are spread throughout the muscle. As a result, stimulation of a single motor unit causes a weak contraction of the *entire* muscle.

The Muscle Twitch

Muscle contraction is easily investigated in the laboratory using an isolated muscle. The muscle is attached to an apparatus that produces a **myogram**, a recording of contractile activity. The line recording the activity is called a *tracing*.

A **muscle twitch** is a motor unit's response to a single action potential of its motor neuron. The muscle fibers contract quickly and then relax. Every twitch myogram has three distinct phases (**Figure 9.14a**).

1. **Latent period.** The **latent period** is the first few milliseconds following stimulation when excitation-contraction coupling is occurring. During this period, cross bridges begin to cycle but muscle tension is not yet measurable and the myogram does not show a response.
2. **Period of contraction.** During the period of contraction, cross bridges are active, from the onset to the peak of tension development, and the myogram tracing rises to a peak. This period lasts 10–100 ms. If the tension (pull) becomes great enough to overcome the resistance of the load, the muscle shortens.
3. **Period of relaxation.** This final phase, lasting 10–100 ms, is initiated by reentry of Ca^{2+} into the SR. Because contractile force is declining, muscle tension decreases to zero and



(a) Axons of motor neurons extend from the spinal cord to the muscle. There each axon divides into a number of axon terminals that form neuromuscular junctions with muscle fibers scattered throughout the muscle.

(b) Branching axon terminals form neuromuscular junctions, one per muscle fiber (photomicrograph 330 \times).

Figure 9.13 A motor unit consists of one motor neuron and all the muscle fibers it innervates. (For a related image, see *A Brief Atlas of the Human Body*, Plate 30.)

the tracing returns to the baseline. If the muscle shortened during contraction, it now returns to its initial length. Notice that a muscle contracts faster than it relaxes, as revealed by the asymmetric nature of the myogram tracing.

As you can see in Figure 9.14b, twitch contractions of some muscles are rapid and brief, as with the muscles controlling eye movements. In contrast, the fibers of fleshy calf muscles (gastrocnemius and soleus) contract more slowly and remain contracted for much longer periods. These differences between muscles reflect variations in enzymes and metabolic properties of the myofibrils.

Graded Muscle Responses

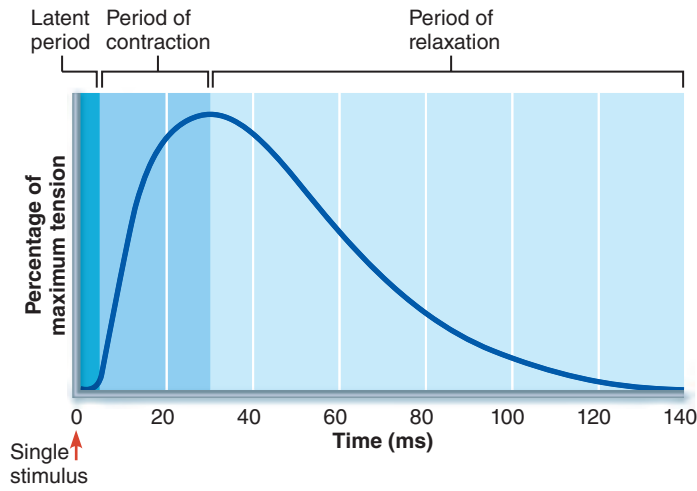
Muscle twitches—like those single, jerky contractions provoked in a laboratory—may result from certain neuromuscular problems, but this is *not* the way our muscles normally operate. Instead, healthy muscle contractions are relatively smooth and vary in strength as different demands are placed on them. These variations, needed for proper control of skeletal movement, are referred to as **graded muscle responses**.

In general, muscle contraction can be graded in two ways: by changing the frequency of stimulation, and by changing the strength of stimulation.

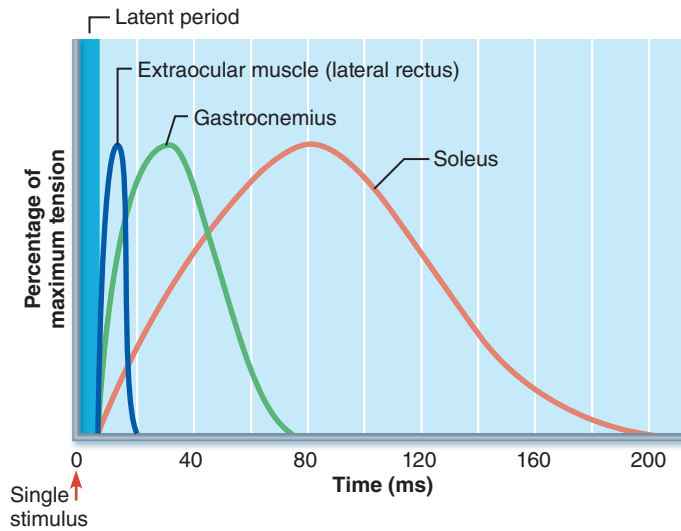
Muscle Response to Changes in Stimulus Frequency The nervous system achieves greater muscular force by increasing the firing rate of motor neurons. For example, if two identical stimuli (electrical shocks or nerve impulses) are delivered to a muscle in rapid succession, the second twitch will be stronger than the first. On a myogram the second twitch will appear to ride on the shoulders of the first (**Figure 9.15a, b**).

This phenomenon, called **wave** or **temporal summation**, occurs because the second contraction occurs before the muscle has completely relaxed. Because the muscle is already partially contracted and more calcium is being squirted into the cytosol to replace that being reclaimed by the SR, muscle tension produced during the second contraction causes more shortening than the first. In other words, the contractions are added together. (However, the refractory period is always honored. Thus, if a second stimulus arrives before repolarization is complete, no wave summation occurs.)

If the stimulus strength is held constant and the muscle is stimulated at an increasingly faster rate: (1) the relaxation time between twitches becomes shorter and shorter, (2) the concentration of Ca^{2+} in the cytosol rises higher and higher, and (3) the degree of wave summation becomes greater and greater, progressing to a sustained but quivering contraction referred to as **unfused** or **incomplete tetanus** (Figure 9.15b).



(a) Myogram showing the three phases of an isometric twitch

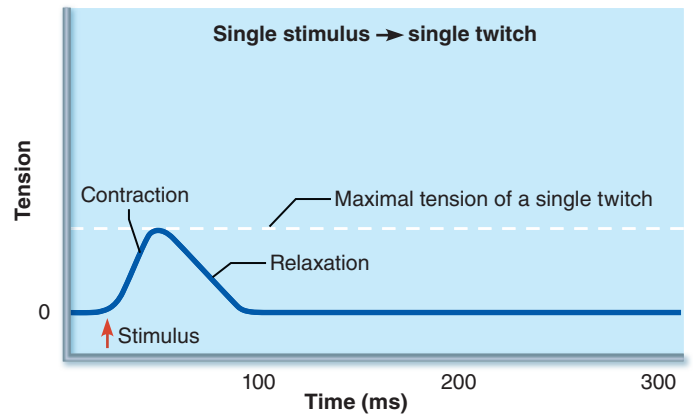


(b) Comparison of the relative duration of twitch responses of three muscles

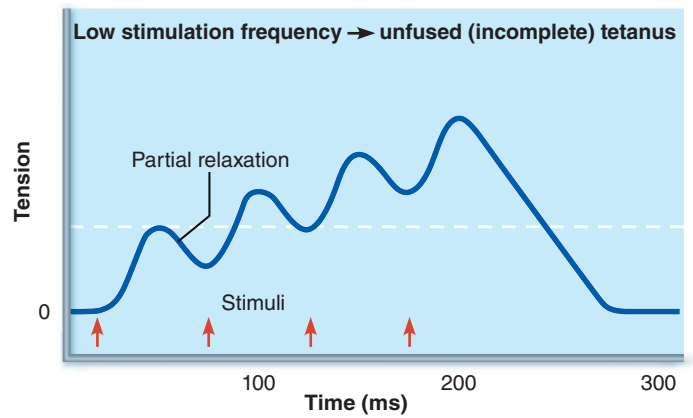
Figure 9.14 The muscle twitch.

Finally, as the stimulation frequency continues to increase, muscle tension increases until it reaches maximal tension. At this point all evidence of muscle relaxation disappears and the contractions fuse into a smooth, sustained contraction plateau called **fused** or **complete tetanus** (tet'ah-nus; *tetan* = rigid, tense) (Figure 9.15c). (Note that this term is often confused with the bacterial disease called tetanus that causes severe involuntary contractions.) In the real world, fused tetanus happens infrequently, for example, when someone shows superhuman strength by lifting a fallen tree limb off a companion.

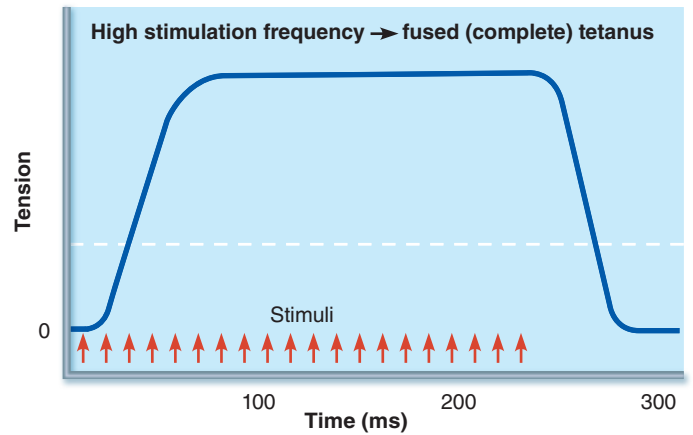
Vigorous muscle activity cannot continue indefinitely. Prolonged tetanus inevitably leads to muscle fatigue, a situation in which the muscle cannot contract and its tension drops to zero.



(a) A single stimulus is delivered. The muscle contracts and relaxes.



(b) If another stimulus is applied before the muscle relaxes completely, then more tension results. This is wave (or temporal) summation and results in unfused (or incomplete) tetanus.



(c) At higher stimulus frequencies, there is no relaxation at all between stimuli. This is fused (complete) tetanus.

Figure 9.15 A muscle's response to changes in stimulation frequency. (Note that tension is measured in grams.)

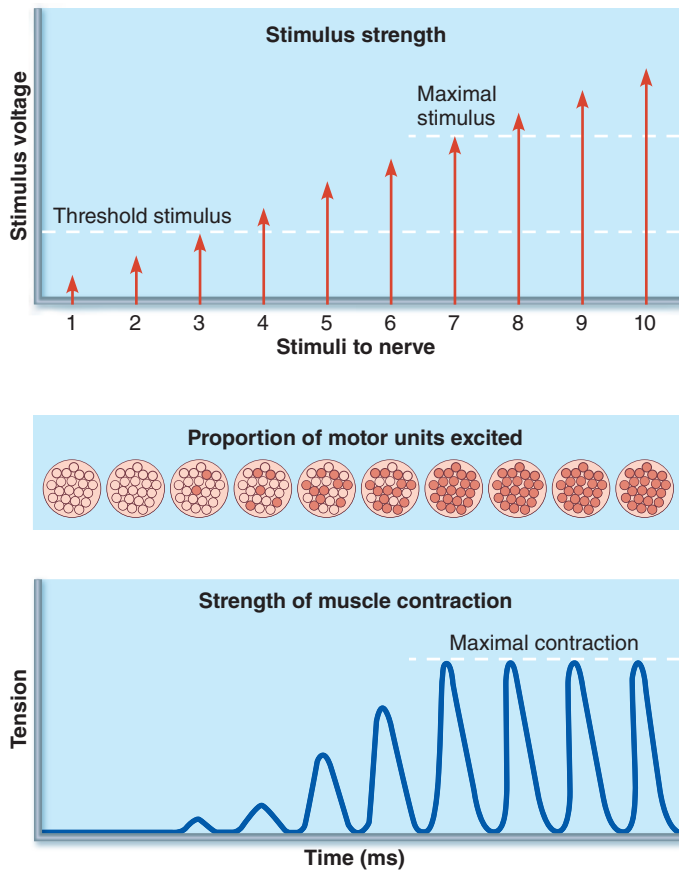


Figure 9.16 Relationship between stimulus intensity (graph at top) and muscle tension (tracing below). Below threshold voltage, the tracing shows no muscle response (stimuli 1 and 2). Once threshold (3) is reached, increases in voltage excite (recruit) more and more motor units until the maximal stimulus is reached (7). Further increases in stimulus voltage produce no further increase in contractile strength.

Muscle Response to Changes in Stimulus Strength Wave summation contributes to contractile force, but its primary function is to produce smooth, continuous muscle contractions by rapidly stimulating a specific number of muscle cells. **Recruitment**, also called **multiple motor unit summation**, controls the force of contraction more precisely. In the laboratory, recruitment is achieved by delivering shocks of increasing voltage to the muscle, calling more and more muscle fibers into play.

- Stimuli that produce no observable contractions are **sub-threshold stimuli**.
- The stimulus at which the first observable contraction occurs is called the **threshold stimulus (Figure 9.16)**. Beyond this point, the muscle contracts more and more vigorously as the stimulus strength increases.
- The **maximal stimulus** is the strongest stimulus that increases contractile force. It represents the point at which all the muscle's motor units are recruited.

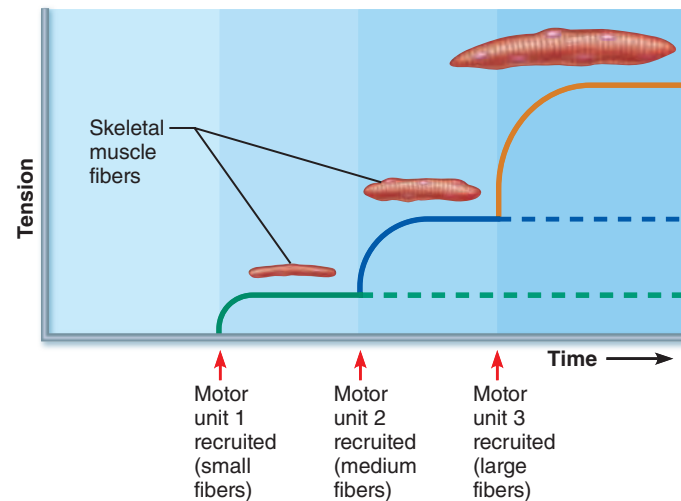


Figure 9.17 The size principle of recruitment. Recruitment of motor neurons controlling skeletal muscle fibers is orderly and follows the size principle.

Increasing the stimulus intensity beyond the maximal stimulus does not produce a stronger contraction. In the body, the same phenomenon is caused by neural activation of an increasingly large number of motor units serving the muscle.

The recruitment process is not random. Instead it is dictated by the *size principle (Figure 9.17)*. In any muscle:

- The motor units with the smallest muscle fibers are activated first because they are controlled by the smallest, most highly excitable motor neurons.
- As motor units with larger and larger muscle fibers begin to be excited, contractile strength increases.
- The largest motor units, containing large, coarse muscle fibers, have as much as 50 times the contractile force of the smallest ones. They are controlled by the largest, least excitable (highest-threshold) neurons and are activated only when the most powerful contraction is necessary.

Why is the size principle important? It allows the increases in force during weak contractions (for example, those that maintain posture or slow movements) to occur in small steps, whereas gradations in muscle force are progressively greater when large amounts of force are needed for vigorous activities such as jumping or running. The size principle explains how the same hand that lightly pats your cheek can deliver a stinging slap at the volleyball during a match.

Although *all* the motor units of a muscle may be recruited simultaneously to produce an exceptionally strong contraction, motor units are more commonly activated asynchronously. At a given instant, some are in tetanus (usually unfused tetanus) while others are resting and recovering. This technique helps prolong a strong contraction by preventing or delaying fatigue. It also explains how weak contractions promoted by infrequent stimuli can remain smooth.

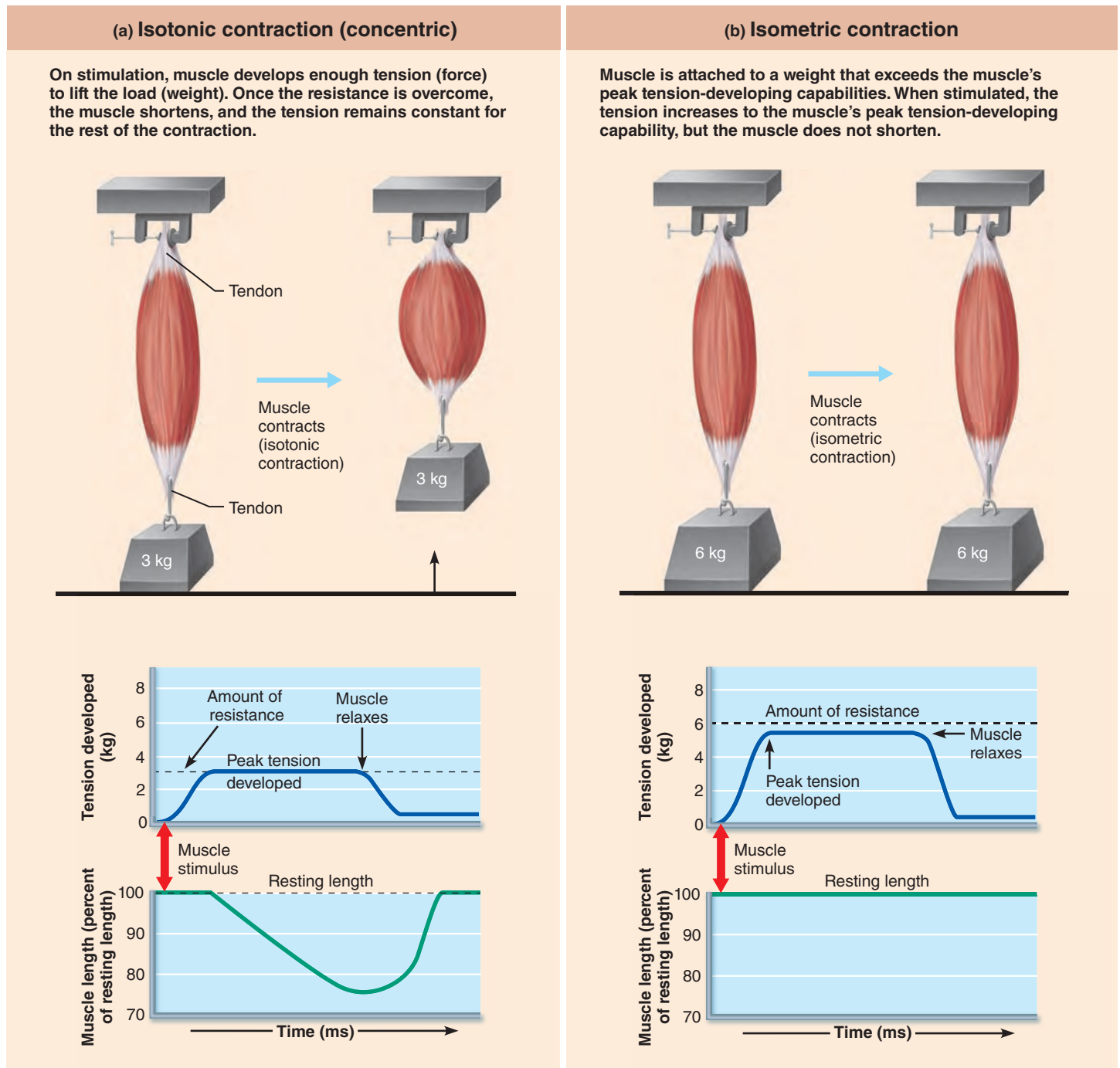


Figure 9.18 Isotonic (concentric) and isometric contractions.

Isotonic and Isometric Contractions

As noted earlier, there are two main categories of contractions—*isotonic* and *isometric*. In **isotonic contractions** (*iso* = same; *ton* = tension), muscle length changes and moves a load. Once sufficient tension has developed to move the load, the tension remains relatively constant through the rest of the contractile period (**Figure 9.18a**).

Isotonic contractions come in two “flavors”—*concentric* and *eccentric*. **Concentric contractions** are those in which the muscle shortens and does work, such as picking up a book or

kicking a ball. Concentric contractions are probably more familiar, but **eccentric contractions**, in which the muscle generates force as it lengthens, are equally important for coordination and purposeful movements.

Eccentric contractions occur in your calf muscle, for example, as you walk up a steep hill. Eccentric contractions are about 50% more forceful than concentric ones at the same load and more often cause delayed-onset muscle soreness. (Consider how your calf muscles *feel* the day after hiking up that hill.) The reason is unclear,

but it may be that the muscle stretching that occurs during eccentric contractions causes microtears in the muscles.

Biceps curls provide a simple example of how concentric and eccentric contractions work together in our everyday activities. When you flex your elbow to raise this textbook to your shoulder, the biceps muscle in your arm is contracting concentrically. When you straighten your arm to return the book to the desktop, the isotonic contraction of your biceps is eccentric. Basically, eccentric contractions put the body in position to contract concentrically. All jumping and throwing activities involve both types of contraction.

In **isometric contractions** (*metric* = measure), tension may build to the muscle's peak tension-producing capacity, but the muscle *neither shortens nor lengthens* (Figure 9.18b). Isometric contractions occur when a muscle attempts to move a load that is greater than the force (tension) the muscle is able to develop—think of trying to lift a piano single-handedly. Muscles contract isometrically when they act primarily to maintain upright posture or to hold joints stationary while movements occur at other joints.

Consider a knee bend. When you squat for a few seconds, the quadriceps muscles of your anterior thigh contract isometrically to hold your knee in the flexed position. When you start to rise to the upright position, they continue to contract isometrically until their tension exceeds the load (weight of your upper body). At that point muscle shortening (concentric contraction) begins. So the quadriceps contractile sequence for a deep knee bend from start to finish is (1) flex knee (eccentric), (2) hold squat position (isometric), (3) extend knee (isometric, then concentric). Of course, this list does not even begin to consider the isometric contractions of the posterior thigh muscles or of the trunk muscles that maintain a relatively erect trunk posture during this movement.

Electrochemical and mechanical events occurring within a muscle are identical in both isotonic and isometric contractions. However, the results are different. In isotonic contractions, the thin filaments slide. In isometric contractions, the cross bridges generate force but do *not* move the thin filaments, so there is no change in the banding pattern from that of the resting state. (You could say that they are “spinning their wheels” on the same actin binding sites.)

Muscle Tone

Skeletal muscles are described as voluntary, but even relaxed muscles are almost always slightly contracted, a phenomenon called **muscle tone**. Muscle tone is due to spinal reflexes that activate first one group of motor units and then another in response to activated stretch receptors in the muscles. Muscle tone does not produce active movements, but it keeps the muscles firm, healthy, and ready to respond to stimulation. Skeletal muscle tone also helps stabilize joints and maintain posture.

✓ Check Your Understanding

10. What is a motor unit?
11. What is happening in the muscle during the latent period of a twitch contraction?
12. Jay is competing in a chin-up competition. What type of muscle contractions are occurring in his biceps muscles

immediately after he grabs the bar? As his body begins to move upward toward the bar? When his body begins to approach the mat?

For answers, see Appendix H.

Muscle Metabolism

- ✓ Describe three ways in which ATP is regenerated during skeletal muscle contraction.
- ✓ Define EPOC and muscle fatigue. List possible causes of muscle fatigue.

Providing Energy for Contraction

As a muscle contracts, ATP supplies the energy to move and detach cross bridges, operate the calcium pump in the SR, and return Na^+ and K^+ to the cell exterior and interior respectively after excitation-contraction coupling. Surprisingly, muscles store very limited reserves of ATP—4 to 6 seconds' worth at most, just enough to get you going. Because ATP is the *only* energy source used directly for contractile activities, it must be regenerated as fast as it is broken down if contraction is to continue.

Fortunately, after ATP is hydrolyzed to ADP and inorganic phosphate in muscle fibers, it is regenerated within a fraction of a second by one or more of the three pathways summarized in **Figure 9.19**: (1) direct phosphorylation of ADP by creatine phosphate, (2) anaerobic glycolysis, which converts glucose to lactic acid, and (3) aerobic respiration. All body cells use glycolysis and aerobic respiration to produce ATP, so we touch on them here but describe them in detail later, in Chapter 24.

Direct Phosphorylation of ADP by Creatine Phosphate (Figure 9.19a) As we begin to exercise vigorously, the demand for ATP soars and consumes the ATP stored in working muscles within a few twitches. Then **creatine phosphate (CP)** (kre' ah-tin), a unique high-energy molecule stored in muscles, is tapped to regenerate ATP while the metabolic pathways adjust to the suddenly higher demand for ATP.

Coupling CP with ADP transfers energy and a phosphate group from CP to ADP to form ATP almost instantly:



Muscle cells store two to three times more CP than ATP. The CP-ADP reaction, catalyzed by the enzyme **creatine kinase**, is so efficient that the amount of ATP in muscle cells changes very little during the initial period of contraction.

Together, stored ATP and CP provide for maximum muscle power for about 15 seconds—long enough to energize a 100-meter dash (slightly longer if the activity is less vigorous). The coupled reaction is readily reversible, and to keep CP “on tap,” CP reserves are replenished during periods of rest or inactivity.

Anaerobic Pathway: Glycolysis and Lactic Acid Formation (Figure 9.19b) As stored ATP and CP are exhausted, more ATP is generated by breaking down (catabolizing) glucose obtained from the blood or glycogen stored in the muscle. The initial phase of glucose breakdown is **glycolysis** (gli-kol'i-sis;

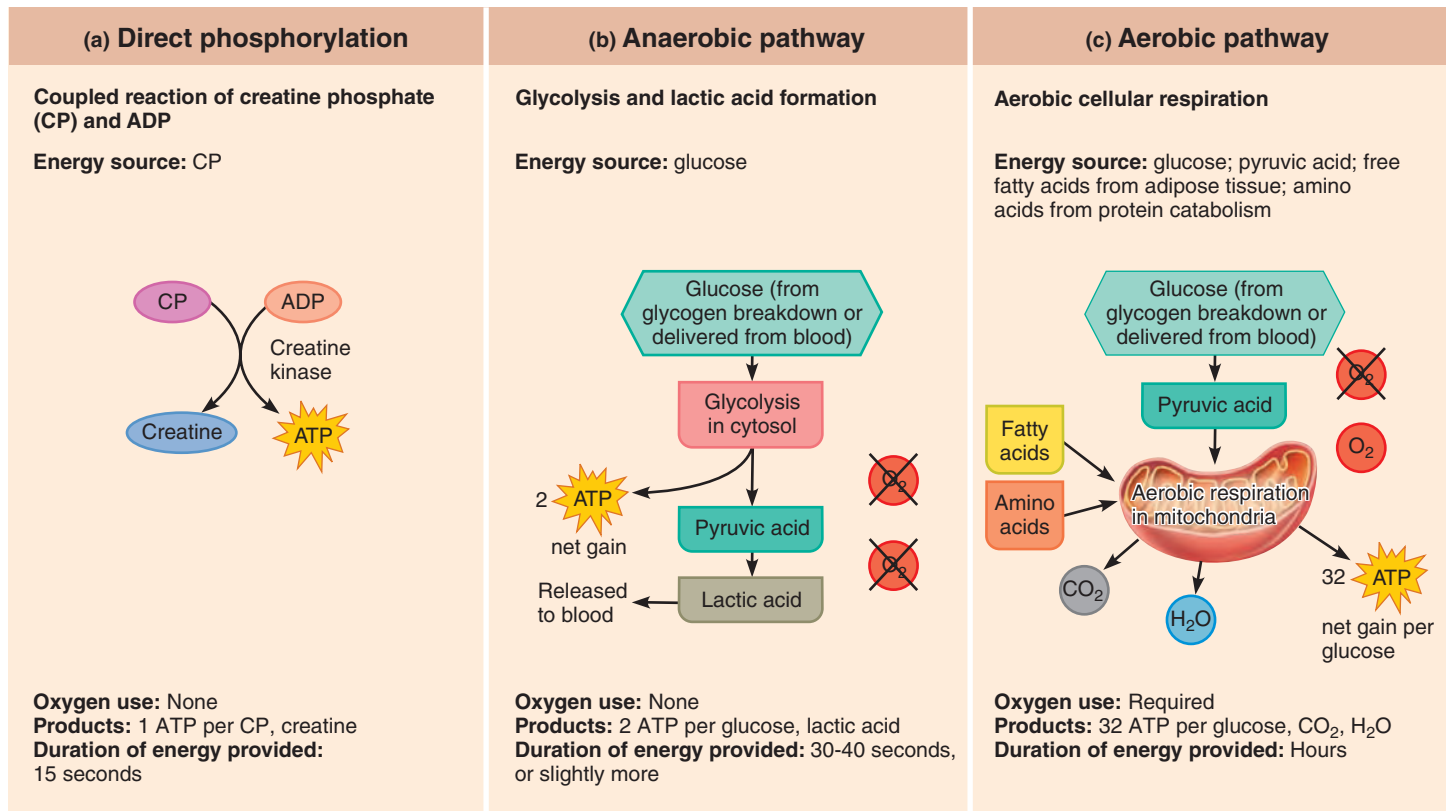


Figure 9.19 Pathways for regenerating ATP during muscle activity. The fastest pathway is direct phosphorylation (a), and the slowest is aerobic respiration (c).

“sugar splitting”). This pathway occurs in both the presence and the absence of oxygen, but because it does not use oxygen, it is an anaerobic (an-a’er-ōb-ik; “without oxygen”) pathway. During glycolysis, glucose is broken down to two *pyruvic acid* molecules, releasing enough energy to form small amounts of ATP (2 ATP per glucose).

Ordinarily, pyruvic acid produced during glycolysis then enters the mitochondria and reacts with oxygen to produce still more ATP in the oxygen-using pathway called aerobic respiration, described shortly. But when muscles contract vigorously and contractile activity reaches about 70% of the maximum possible (for example, when you run 600 meters with maximal effort), the bulging muscles compress the blood vessels within them, impairing blood flow and oxygen delivery. Under these anaerobic conditions, most of the pyruvic acid produced during glycolysis is converted into **lactic acid**, and the overall process is referred to as **anaerobic glycolysis**. Thus, during oxygen deficit, lactic acid is the end product of cellular metabolism of glucose.

Most of the lactic acid diffuses out of the muscles into the bloodstream. Subsequently, the liver, heart, or kidney cells pick up the lactic acid and use it as an energy source. Additionally, liver cells can reconvert it to pyruvic acid or glucose and release it back into the bloodstream for muscle use, or convert it to glycogen for storage.

The anaerobic pathway harvests only about 5% as much ATP from each glucose molecule as the aerobic pathway, but it produces ATP about 2½ times faster. For this reason, when large amounts

of ATP are needed for moderate periods (30–40 seconds) of strenuous muscle activity, glycolysis can provide most of the ATP needed as long as the required fuels and enzymes are available. Together, stored ATP and CP and the glycolysis–lactic acid pathway can support strenuous muscle activity for nearly a minute.

Although anaerobic glycolysis readily fuels spurts of vigorous exercise, it has shortcomings. Huge amounts of glucose are used to produce relatively small harvests of ATP, and the accumulating lactic acid is partially responsible for muscle soreness during intense exercise.

Aerobic Respiration (Figure 9.19c) Because the amount of creatine phosphate is limited, muscles must metabolize nutrients to transfer energy from foodstuffs to ATP. During rest and light to moderate exercise, even if prolonged, 95% of the ATP used for muscle activity comes from aerobic respiration. **Aerobic respiration** occurs in the mitochondria, requires oxygen, and involves a sequence of chemical reactions that break the bonds of fuel molecules and release energy to make ATP.

Aerobic respiration, which includes glycolysis and the reactions that take place in the mitochondria, breaks down glucose entirely. Water, carbon dioxide, and large amounts of ATP are its final products.



The carbon dioxide released diffuses out of the muscle tissue into the blood, to be removed from the body by the lungs.

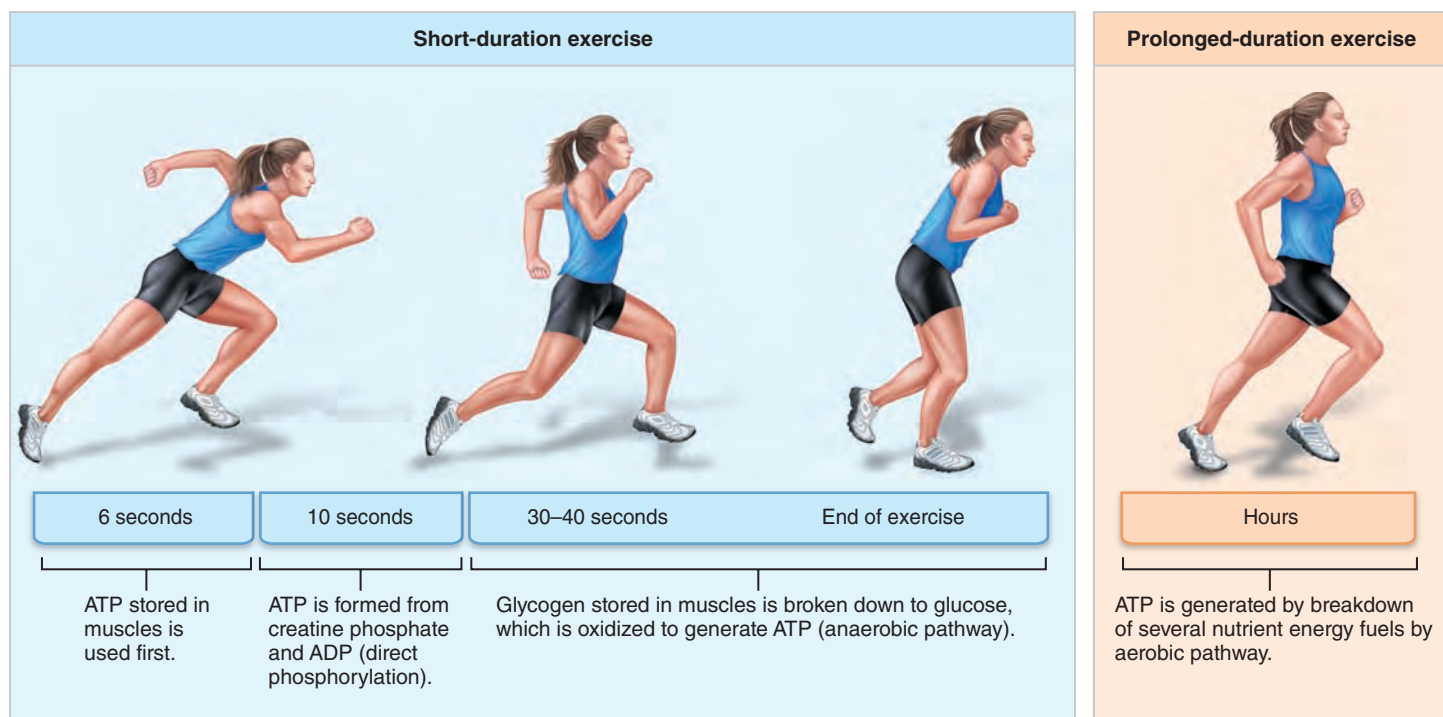


Figure 9.20 Comparison of energy sources used during short-duration exercise and prolonged-duration exercise.

As exercise begins, muscle glycogen provides most of the fuel. Shortly thereafter, bloodborne glucose, pyruvic acid from glycolysis, and free fatty acids are the major sources of fuels. After about 30 minutes, fatty acids become the major energy fuels. Aerobic respiration provides a high yield of ATP (about 32 ATP per glucose), but it is slow because of its many steps and it requires continuous delivery of oxygen and nutrient fuels to keep it going.

Energy Systems Used During Sports Which pathways predominate during exercise? As long as a muscle cell has enough oxygen, it will form ATP by the aerobic pathway. When ATP demands are within the capacity of the aerobic pathway, light to moderate muscular activity can continue for several hours in well-conditioned individuals (Figure 9.20). However, when exercise demands begin to exceed the ability of the muscle cells to carry out the necessary reactions quickly enough, anaerobic pathways begin to contribute more and more of the total ATP generated. The length of time a muscle can continue to contract using aerobic pathways is called **aerobic endurance**, and the point at which muscle metabolism converts to anaerobic glycolysis is called **anaerobic threshold**.

Activities that require a surge of power but last only a few seconds, such as weight lifting, diving, and sprinting, rely entirely on ATP and CP stores. The more on-and-off or burstlike activities of tennis, soccer, and a 100-meter swim appear to be fueled almost entirely by anaerobic glycolysis (Figure 9.20). Prolonged activities such as marathon runs and jogging, where endurance rather than power is the goal, depend mainly on aerobic respiration using both glucose and fatty acids as fuels.

Levels of CP and ATP don't change much during prolonged exercise because ATP is generated at the same rate as it is used—a “pay as you go” system. Compared to anaerobic energy production, aerobic generation of ATP is relatively slow, but the ATP harvest is enormous.

Muscle Fatigue

Muscle fatigue is a state of *physiological inability to contract* even though the muscle still may be receiving stimuli. Although many factors appear to contribute to fatigue, its specific causes are not fully understood. Most experimental evidence indicates that fatigue is due to a problem in excitation-contraction coupling or, in rare cases, problems at the neuromuscular junction. Availability of ATP declines during contraction, but it is abnormal for a muscle to totally run out of ATP. So, lack of ATP is not a fatigue-producing factor in moderate exercise.

Several ionic imbalances contribute to muscle fatigue. As action potentials are transmitted, potassium is lost from the muscle cells, and accumulates in the fluids of the T tubules. This ionic change disturbs the membrane potential of the muscle cells and halts Ca^{2+} release from the SR.

Theoretically, in short-duration exercise, an accumulation of inorganic phosphate (P_i) from CP and ATP breakdown may interfere with calcium release from the SR. Alternatively, it may interfere with the release of P_i from myosin and thus hamper myosin's power strokes. Lactic acid has long been assumed to be a major cause of fatigue, and excessive intracellular accumulation of lactic acid (which causes the muscles to ache) raises the concentration of H^+ and alters contractile proteins. However, pH is

normally regulated within normal limits in all but the greatest degree of exertion. Additionally, lactic acid actually counteracts high K^+ levels, which do lead to muscle fatigue (as noted above).

In general, intense exercise of short duration produces fatigue rapidly via ionic disturbances that alter E-C coupling, but recovery is also rapid. In contrast, the slow-developing fatigue of prolonged low-intensity exercise may require several hours for complete recovery. It appears that this type of exercise damages the SR, interfering with Ca^{2+} regulation and release, and therefore with muscle activation.

Excess Postexercise Oxygen Consumption (EPOC)

Whether or not fatigue occurs, vigorous exercise alters a muscle's chemistry dramatically. For a muscle to return to its resting state, all the following must occur:

- Its oxygen reserves in myoglobin must be replenished.
- The accumulated lactic acid must be reconverted to pyruvic acid.
- Glycogen stores must be replaced.
- ATP and creatine phosphate reserves must be resynthesized.

The use of these muscle stores during anaerobic exercise simply defers when the oxygen is consumed, because replacing them requires oxygen uptake and aerobic metabolism after exercise ends. Additionally, the liver must convert any lactic acid persisting in blood to glucose or glycogen. Once exercise stops, the repayment process begins.

The extra amount of oxygen that the body must take in for these restorative processes is called the **excess postexercise oxygen consumption (EPOC)**, formerly called the oxygen debt. EPOC represents the difference between the amount of oxygen needed for totally aerobic muscle activity and the amount actually used. All anaerobic sources of ATP used during muscle activity contribute to EPOC.

Heat Production During Muscle Activity

Only about 40% of the energy released during muscle contraction is converted to useful work (still, this percentage is significantly higher than that of many mechanical devices). The rest is given off as heat, which has to be dealt with to maintain body homeostasis.

When you exercise vigorously, you start to feel hot as the liberated heat warms your blood. Like a car's cooling system that dissipates heat, several homeostatic processes prevent heat in the body from building to dangerous levels. These processes include sweating and radiating heat from the skin surface.

Shivering represents the opposite side of homeostatic balance. In this case the body is too cold and muscle contractions are used to produce more heat.

✓ Check Your Understanding

13. When Eric returned from jogging, he was breathing heavily, sweating profusely, and complained that his legs ached and felt weak. His wife poured him a sports drink and urged him to take it easy until he could "catch his breath." On the basis of what you have learned about muscle energy metabolism, respond to the following questions: Why is Eric breathing heavily? Which

ATP-generating pathway have his working muscles been using that makes him breathless? What metabolic products might account for his sore muscles and muscle weakness?

For answers, see Appendix H.

Force of Muscle Contraction

- ✓ Describe factors that influence the force, velocity, and duration of skeletal muscle contraction.
- ✓ Describe three types of skeletal muscle fibers and explain the relative value of each type.

The force of muscle contraction depends on the number of myosin cross bridges that are attached. This in turn is affected by four factors (**Figure 9.21**): (1) number of muscle fibers stimulated, (2) relative size of the fibers, (3) frequency of stimulation, and (4) degree of muscle stretch. Let's examine the role of each factor.

Number of Muscle Fibers Recruited

As already discussed, the more motor units that are recruited, the greater the muscle force.

Size of Muscle Fibers

The bulkier the muscle (the greater its cross-sectional area), the more tension it can develop and the greater its strength, but there is more to it than this. As noted earlier, the large fibers of large motor units produce the most powerful movements. Regular resistance exercise increases muscle force by causing muscle cells to *hypertrophy* (hi-per'tro-fe), or increase in size.

Frequency of Stimulation

As a muscle begins to contract, the force generated by the cross bridges—the **internal tension**—stretches the connective tissue sheaths (noncontractile components). These in turn become taut and transfer their tension, called the **external tension**, to the load

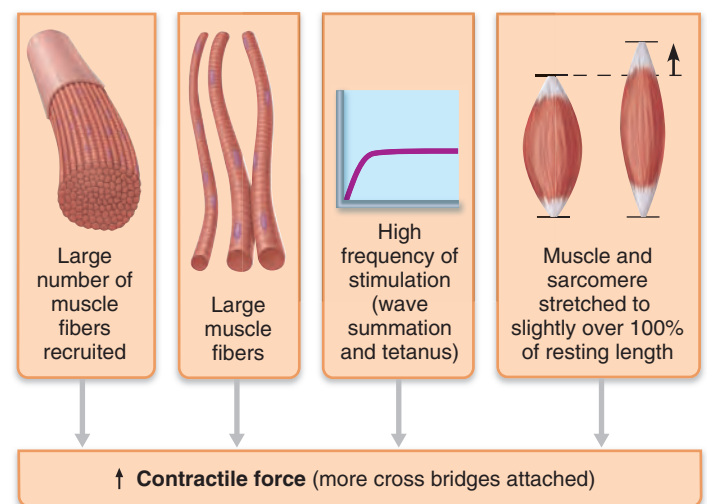
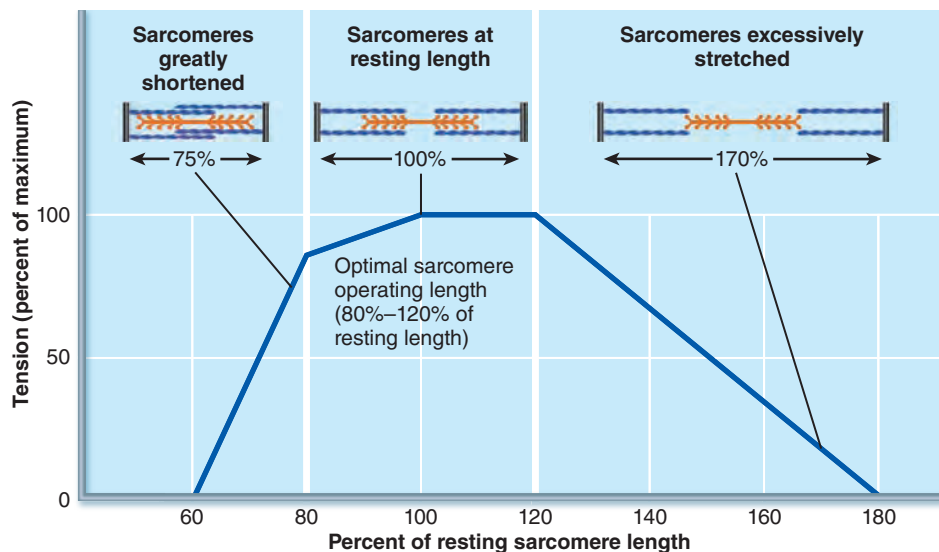


Figure 9.21 Factors that increase the force of skeletal muscle contraction.

Figure 9.22 Length-tension relationships of sarcomeres in skeletal muscles. A muscle generates maximum force when it is between 80 and 120% of its optimal resting length. Increases and decreases beyond this optimal range reduce its force and ability to generate tension.



(muscle insertion). When the contraction ends, the noncontractile components recoil and help return the muscle to its resting length.

Time is required to take up slack and stretch the noncontractile components, and while this is happening, the internal tension is already declining. So, in brief twitch contractions, the external tension is always less than the internal tension. However, when a muscle is stimulated rapidly, contractions are summed, becoming stronger and more vigorous and ultimately producing tetanus (see Figure 9.15).

During tetanic contractions more time is available to stretch the noncontractile components, and external tension approaches the internal tension. So, the more rapidly a muscle is stimulated, the greater the force it exerts.

Degree of Muscle Stretch

The optimal operating length for a muscle fiber is the length at which it can generate maximum force (Figure 9.21 and Figure 9.22). Within a sarcomere, the ideal **length-tension relationship** occurs when a muscle is slightly stretched and the thin and thick filaments overlap optimally, because this relationship permits sliding along nearly the entire length of the thin filaments.

If a muscle fiber stretches so much that the filaments do not overlap, the myosin heads have nothing to attach to and cannot generate tension. Alternatively, if the sarcomeres are so compressed and cramped that the Z discs abut the thick myofilaments, and the thin filaments touch and interfere with one another, little or no further shortening can occur.

If you stretch a muscle to various extents and stimulate it tetanically, the active tension the muscle can generate varies with length (Figure 9.22). A severely stretched muscle (say one over 180% of its optimal length) cannot develop tension. Likewise, at 75% of a muscle's resting length, its ability to generate force (or shorten) is limited because the actin myofilaments in its sarcomeres overlap and the thick filaments run into the Z discs, restricting further shortening.

In the body, skeletal muscles are maintained near their optimal operating length by the way they are attached to bones. The

joints normally prevent bone movements that would stretch attached muscles beyond their optimal range.

Velocity and Duration of Contraction

Muscles vary in how fast they can contract and how long they can continue to contract before they fatigue. These characteristics are influenced by muscle fiber type, load, and recruitment.

Muscle Fiber Type

There are several ways of classifying muscle fibers, but learning about these classes will be easier if you pay attention to just two functional characteristics:

- **Speed of contraction.** On the basis of speed (velocity) of fiber shortening, there are **slow fibers** and **fast fibers**. The difference reflects how fast their myosin ATPases split ATP, and the pattern of electrical activity of their motor neurons. Contraction duration also varies with fiber type and depends on how quickly Ca^{2+} moves from the cytosol into the SR.
- **Major pathways for forming ATP.** The cells that rely mostly on the oxygen-using aerobic pathways for ATP generation are **oxidative fibers**. Those that rely more on anaerobic glycolysis are **glycolytic fibers**.

Using these two criteria, we can classify skeletal muscle cells as: **slow oxidative fibers**, **fast oxidative fibers**, or **fast glycolytic fibers**.

Table 9.2 gives details about each group, but a word to the wise: Do not approach this information by rote memorization—you'll just get frustrated. Instead, start with what you know for any category and see how the characteristics listed support that.

For example, think about a *slow oxidative fiber* (Table 9.2, first column, and Figure 9.23, right side). We can see that it

- Contracts *slowly* because its myosin ATPases are slow (a criterion)
- Depends on *oxygen* delivery and aerobic pathways (its major pathways for forming ATP give it *high oxidative capacity*—a criterion)

- Resists fatigue and has high endurance (typical of fibers that depend on aerobic metabolism)
- Is thin (a large amount of cytoplasm impedes diffusion of O_2 and nutrients from the blood)
- Has relatively little power (a thin cell can contain only a limited number of myofibrils)
- Has many mitochondria (actual sites of oxygen use)
- Has a rich capillary supply (the better to deliver bloodborne O_2)
- Is red (its color stems from an abundant supply of myoglobin, muscle's oxygen-binding pigment that stores O_2 reserves in the cell and helps O_2 diffuse through the cell)

Add these features together and you have a muscle fiber best suited to endurance-type activities.

Now think about a *fast glycolytic fiber* (Table 9.2, third column, and Figure 9.23, left side). In contrast, it

- Contracts *rapidly* due to the activity of fast myosin ATPases
- Does not use oxygen
- Depends on plentiful *glycogen* reserves for fuel rather than on blood-delivered nutrients
- Tires quickly because glycogen reserves are short-lived and lactic acid accumulates quickly, making it a fatigable fiber
- Has a large diameter, indicating the plentiful myofilaments that allow it to contract powerfully before it “poops out”

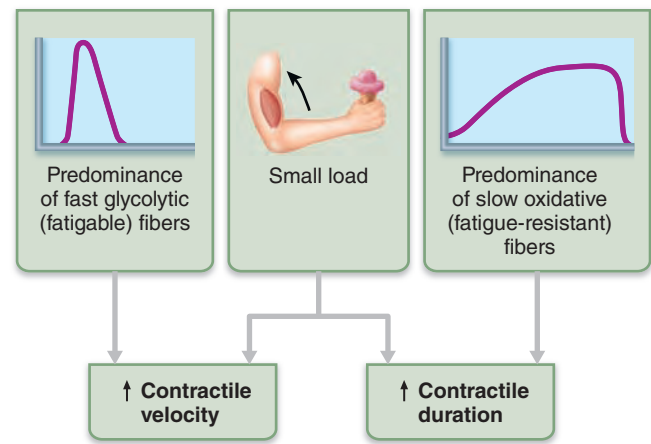


Figure 9.23 Factors influencing velocity and duration of skeletal muscle contraction.

- Has few mitochondria, little myoglobin and few capillaries (making it white), and is a much thicker cell (because it doesn't depend on continuous oxygen and nutrient diffusion from the blood)

For these reasons, a fast glycolytic fiber is best suited for short-term, rapid, intense movements (moving furniture across the room, for example).

Table 9.2 Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers

	SLOW OXIDATIVE FIBERS	FAST OXIDATIVE FIBERS	FAST GLYCOLYTIC FIBERS
Metabolic Characteristics			
Speed of contraction	Slow	Fast	Fast
Myosin ATPase activity	Slow	Fast	Fast
Primary pathway for ATP synthesis	Aerobic	Aerobic (some anaerobic glycolysis)	Anaerobic glycolysis
Myoglobin content	High	High	Low
Glycogen stores	Low	Intermediate	High
Recruitment order	First	Second	Third
Rate of fatigue	Slow (fatigue-resistant)	Intermediate (moderately fatigue-resistant)	Fast (fatigable)
Activities Best Suited For			
	Endurance-type activities—e.g., running a marathon; maintaining posture (antigravity muscles)	Sprinting, walking	Short-term intense or powerful movements, e.g., hitting a baseball
Structural Characteristics			
Color	Red	Red to pink	White (pale)
Fiber diameter	Small	Intermediate	Large
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few

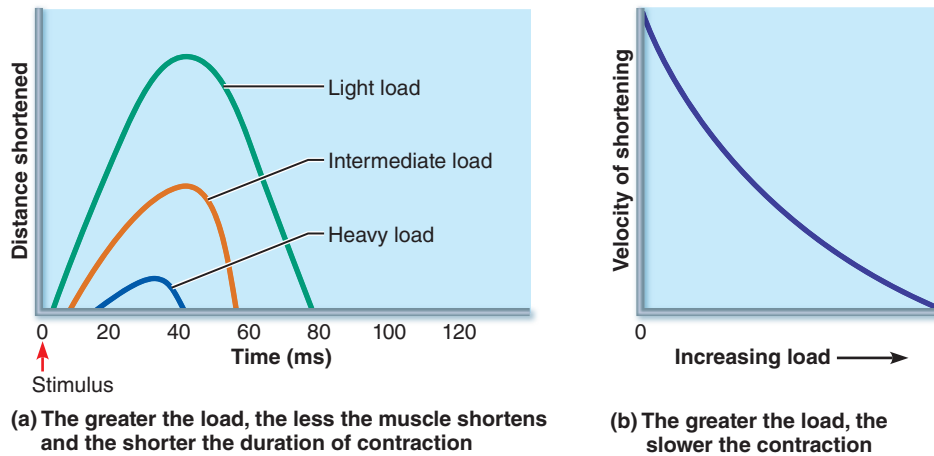


Figure 9.24 Influence of load on duration and velocity of muscle contraction.

Finally, consider the less common intermediate muscle fiber types, called *fast oxidative fibers* (Table 9.2, middle column). They have many characteristics intermediate between the other two types (fiber diameter and power, for example). Like fast glycolytic fibers, they contract quickly, but like slow oxidative fibers, they are oxygen dependent and have a rich supply of myoglobin and capillaries.

Some muscles have a predominance of one fiber type, but most contain a mixture of fiber types, which gives them a range of contractile speeds and fatigue resistance. For example, a calf muscle can propel us in a sprint (using its white fast glycolytic fibers) or a long-distance race (making good use of its slow and fast oxidative fibers). But, as might be expected, all muscle fibers in a particular *motor unit* are of the same type.

Although everyone's muscles contain mixtures of the three fiber types, some people have relatively more of one kind. These differences are genetically initiated, but can be modified by exercise and no doubt determine athletic capabilities, such as endurance versus strength, to a large extent. For example, muscles of marathon runners have a high percentage of slow oxidative fibers (about 80%), while those of sprinters contain a higher percentage (about 60%) of fast oxidative and glycolytic fibers. Interconversion between the “fast” fiber types occurs as a result of specific exercise regimes, as we'll describe below.

Load

Because muscles are attached to bones, they are always pitted against some resistance, or load, when they contract. As you might expect, they contract fastest when there is no added load on them. A greater load results in a longer latent period, a slower contraction, and a shorter duration of contraction (**Figure 9.24**). If the load exceeds the muscle's maximum tension, the speed of shortening is zero and the contraction is isometric (see Figure 9.18b).

Recruitment

In the same way that many hands on a project can get a job done more quickly and also can keep working longer, the more motor units that are contracting, the faster and more prolonged the contraction.

✓ Check Your Understanding

- List two factors that influence contractile force and two that influence velocity of contraction.
- Jim called several friends to help him move. Would he prefer to have those with more slow oxidative muscle fibers or those with more fast glycolytic fibers as his helpers? Why?

For answers, see Appendix H.

Adaptations to Exercise

- ✓ Compare and contrast the effects of aerobic and resistance exercise on skeletal muscles and on other body systems.

The amount of work a muscle does is reflected in changes in the muscle itself. When used actively or strenuously, muscles may become larger or stronger, or more efficient and fatigue resistant. Inactivity, on the other hand, *always* leads to muscle weakness and wasting.

Aerobic (Endurance) Exercise

Aerobic, or **endurance**, **exercise** such as swimming, jogging, fast walking, and biking results in several recognizable changes in skeletal muscles:

- The number of capillaries surrounding the muscle fibers increases.
- The number of mitochondria within the muscle fibers also increases.
- The fibers synthesize more myoglobin.

These changes occur in all fiber types, but are most dramatic in slow oxidative fibers, which depend primarily on aerobic pathways. The changes result in more efficient muscle metabolism and in greater endurance, strength, and resistance to fatigue. Additionally, regular endurance exercise may convert fast glycolytic fibers into fast oxidative fibers.

Resistance Exercise

The moderately weak but sustained muscle activity required for endurance exercise does not promote significant skeletal muscle hypertrophy, even though the exercise may go on for hours. Muscle hypertrophy—think of the bulging biceps and chest muscles of a professional weight lifter—results mainly from high-intensity **resistance exercise** (typically under anaerobic conditions) such as weight lifting or isometric exercise, which pits muscles against high-resistance or immovable forces. Here strength, not stamina, is important, and a few minutes every other day is sufficient to allow a proverbial weakling to put on 50% more muscle within a year.

The additional muscle bulk largely reflects the increased size of individual muscle fibers (particularly the fast glycolytic variety) rather than an increased number of muscle fibers. [However, some of the bulk may result from longitudinal splitting of the fibers and subsequent growth of these “split” cells, or from the proliferation and fusion of satellite cells (see p. 312). The controversy is still raging.] Vigorously stressed muscle fibers also contain more mitochondria, form more myofilaments and myofibrils, store more glycogen, and develop more connective tissue between muscle cells.

Collectively these changes promote significant increases in muscle strength and size. Resistance activities can also convert fast oxidative fibers to fast glycolytic fibers. However, if the specific exercise routine is discontinued, the converted fibers revert to their original metabolic properties.

Resistance training can produce incredibly bulging muscles, but if done unwisely, some muscles may develop more than others. Because muscles work in antagonistic pairs or groups, opposing muscles must be equally strong to work together smoothly. When muscle training is not balanced, individuals can become *muscle-bound*, which means they lack flexibility, have a generally awkward stance, and are unable to make full use of their muscles.

A Balanced Exercise Program

Whatever the activity, exercise gains adhere to the *overload principle*. Forcing a muscle to work hard increases muscle strength and endurance. As muscles adapt to these greater demands, they must be overloaded even more to produce further gains.

However, always follow a heavy-workout day with a day of rest or an easy workout to let your muscles recover and repair themselves. Doing too much too soon, or ignoring the warning signs of muscle or joint pain, increases your risk of **overuse injuries** that may lead to lifetime disability.

Endurance and resistance exercises produce different patterns of muscular response, so it is important to know what your exercise goals are. Lifting weights will not improve your endurance for a triathlon. By the same token, jogging will do little to improve your muscle definition or enhance your strength for moving furniture. A program that alternates aerobic and anaerobic activities provides the best balance for optimal health.



Homeostatic Imbalance 9.3

To remain healthy, muscles must be active. Immobilization due to enforced bed rest or loss of neural stimulation results in *disuse atrophy* (degeneration and loss of mass), which begins almost as

soon as the muscles are immobilized. Under such conditions, muscle strength can decline at the rate of 5% per day!

As noted earlier, even at rest, muscles receive weak intermittent stimuli from the nervous system. When totally deprived of neural stimulation, a paralyzed muscle may atrophy to one-quarter of its initial size. Fibrous connective tissue replaces the lost muscle tissue, making muscle rehabilitation impossible. +

✓ Check Your Understanding

16. How do aerobic and resistance exercise differ in their effects on muscle size and function?

For answers, see Appendix H.

Smooth Muscle

- ✓ Compare the gross and microscopic anatomy of smooth muscle cells to that of skeletal muscle cells.
- ✓ Compare and contrast the contractile mechanisms and the means of activation of skeletal and smooth muscles.
- ✓ Distinguish between unitary and multi unit smooth muscle structurally and functionally.

Except for the heart, which is made of cardiac muscle, the muscle in the walls of all the body's hollow organs is almost entirely smooth muscle. The chemical and mechanical events of contraction are essentially the same in all muscle tissues, but smooth muscle is distinctive in several ways, as summarized in **Table 9.3** on p. 310.

Microscopic Structure of Smooth Muscle Fibers

Smooth muscle fibers are spindle-shaped cells of variable size, each with one centrally located nucleus (**Figure 9.25b**). Typically, they have a diameter of 5–10 μm and are 30–200 μm long. Skeletal muscle fibers are up to 10 times wider and thousands of times longer.

Smooth muscle lacks the coarse connective tissue sheaths seen in skeletal muscle. However, a small amount of fine connective tissue (endomysium), secreted by the smooth muscles themselves and containing blood vessels and nerves, is found between smooth muscle fibers.

Most smooth muscle is organized into sheets of closely apposed fibers. These sheets occur in the walls of all but the smallest blood vessels and in the walls of hollow organs of the respiratory, digestive, urinary, and reproductive tracts. In most cases, there are two sheets of smooth muscle with their fibers oriented at right angles to each other, as in the intestine (**Figure 9.25**).

- In the *longitudinal layer*, the muscle fibers run parallel to the long axis of the organ. Consequently, when these fibers contract, the organ dilates and shortens.

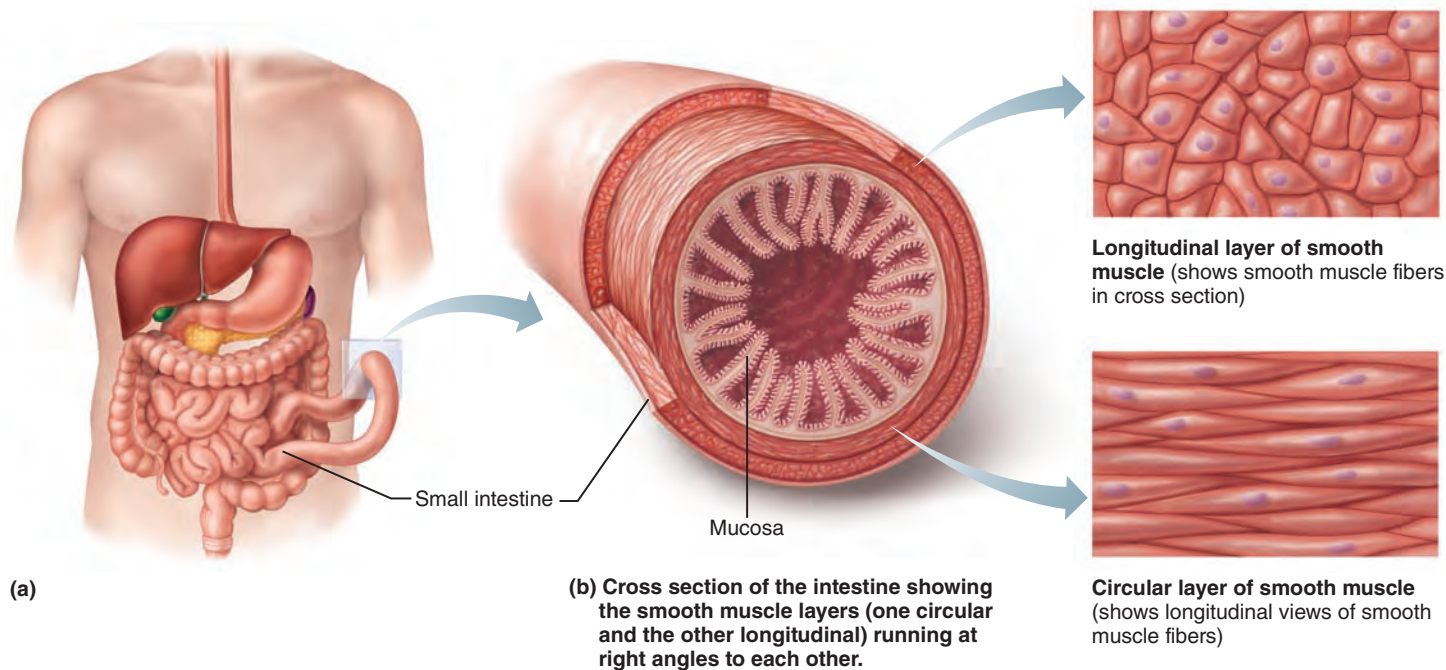


Figure 9.25 Arrangement of smooth muscle in the walls of hollow organs.

- In the *circular layer*, the fibers run around the circumference of the organ. Contraction of this layer constricts the lumen of the organ and elongates the organ.

The alternating contraction and relaxation of these layers mixes substances in the lumen and squeezes them through the organ's internal pathway. This propulsive action is called **peristalsis** (per"i-stal'sis; "around contraction"). Contraction of smooth muscle in the rectum, urinary bladder, and uterus helps those organs to expel their contents. Smooth muscle contraction also accounts for the constricted breathing of asthma and for stomach cramps.

Smooth muscle lacks the highly structured neuromuscular junctions of skeletal muscle. Instead, the innervating nerve fibers, which are part of the autonomic (involuntary) nervous system, have numerous bulbous swellings, called **varicosities** (Figure 9.26). The varicosities release neurotransmitter into a wide synaptic cleft in the general area of the smooth muscle cells. Such junctions are called **diffuse junctions**. Comparing the neural input to skeletal and smooth muscles, you could say that skeletal muscle gets priority mail while smooth muscle gets bulk mailings.

The sarcoplasmic reticulum of smooth muscle fibers is much less developed than that of skeletal muscle and lacks a specific pattern relative to the myofilaments. Some SR tubules of smooth muscle touch the sarcolemma at several sites, forming what resembles half-triads that may couple the action potential to calcium release from the SR.

T tubules are absent, but the sarcolemma has multiple **caveolae**, pouchlike infoldings that sequester bits of extracellular fluid containing a high concentration of Ca^{2+} close to the membrane (Figure 9.27a). Consequently, when calcium channels in the

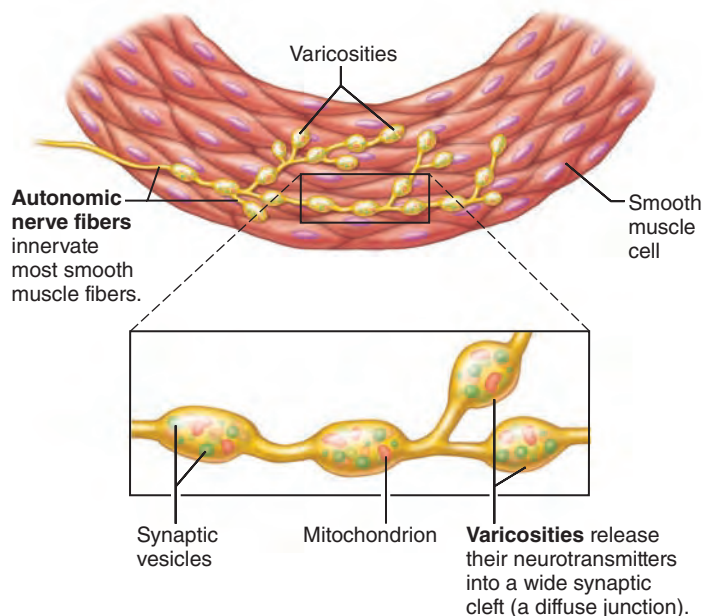


Figure 9.26 Innervation of smooth muscle.

caveolae open, Ca^{2+} influx occurs rapidly. Although the SR *does* release some of the calcium that triggers contraction, most Ca^{2+} enters through calcium channels directly from the extracellular space. This situation is quite different from what we see in skeletal muscle, which does not depend on extracellular Ca^{2+} for excitation-contraction coupling. Contraction ends when cytoplasmic calcium is actively transported into the SR and out of the cell.

There are no striations in smooth muscle, as its name indicates, and therefore no sarcomeres. Smooth muscle fibers do contain interdigitating thick and thin filaments, but the myosin filaments are a lot shorter than the actin filaments and the type of myosin contained differs from skeletal muscle. The proportion and organization of smooth muscle myofilaments differ from skeletal muscle in the following ways:

- **Thick filaments are fewer but have myosin heads along their entire length.** The ratio of thick to thin filaments is much lower in smooth muscle than in skeletal muscle (1:13 compared to 1:2). However, thick filaments of smooth muscle contain actin-gripping myosin heads along their *entire length*, a feature that makes smooth muscle as powerful as a skeletal muscle of the same size. Also, in smooth muscle the myosin heads are oriented in one direction on one side of the filament and in the opposite direction on the other side.
- **No troponin complex in thin filaments.** As in skeletal muscle, tropomyosin mechanically stabilizes the thin filaments, but smooth muscle has no calcium-binding troponin complex. Instead, a protein called *calmodulin* acts as the calcium-binding site.
- **Thick and thin filaments arranged diagonally.** Bundles of contractile proteins crisscross within the smooth muscle cell so they spiral down the long axis of the cell like the stripes on a barber pole. Because of this diagonal arrangement, the smooth muscle cells contract in a twisting way so that they look like tiny corkscrews (Figure 9.27b).
- **Intermediate filament–dense body network.** Smooth muscle fibers contain a lattice-like arrangement of noncontractile *intermediate filaments* that resist tension. They attach at regular intervals to cytoplasmic structures called **dense bodies** (Figure 9.27). The **dense bodies**, which are also tethered to the sarcolemma, act as anchoring points for thin filaments and therefore correspond to Z discs of skeletal muscle.

The intermediate filament–dense body network forms a strong, cable-like intracellular cytoskeleton that harnesses the pull generated by the sliding of the thick and thin filaments. During contraction, areas of the sarcolemma between the dense bodies bulge outward, making the cell look puffy (Figure 9.27b). Dense bodies at the sarcolemma surface also bind the muscle cell to the connective tissue fibers outside the cell (endomysium) and to adjacent cells. This arrangement transmits the pulling force to the surrounding connective tissue and partly accounts for the synchronous contractions of most smooth muscle.

Contraction of Smooth Muscle

Mechanism of Contraction

In most cases, adjacent smooth muscle fibers exhibit slow, synchronized contractions, the whole sheet responding to a stimulus in unison. This synchronization reflects electrical coupling of smooth muscle cells by *gap junctions*, specialized cell connections described in Chapter 3. Skeletal muscle fibers are electrically isolated from one another, each stimulated to contract by its own neuromuscular junction. By contrast, gap junctions

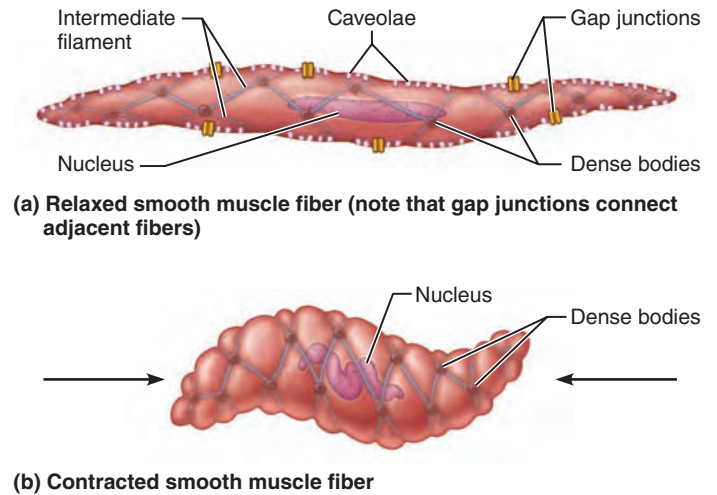


Figure 9.27 Intermediate filaments and dense bodies of smooth muscle fibers harness the pull generated by myosin cross bridges. Intermediate filaments attach to dense bodies throughout the sarcoplasm.

allow smooth muscles to transmit action potentials from fiber to fiber.

Some smooth muscle fibers in the stomach and small intestine are *pacemaker cells*: Once excited, they act as “drummers” to set the pace of contraction for the entire muscle sheet. These pacemakers have fluctuating membrane potentials and are self-excitatory, that is, they depolarize spontaneously in the absence of external stimuli. However, neural and chemical stimuli can modify both the rate and the intensity of smooth muscle contraction.

Contraction in smooth muscle is like contraction in skeletal muscle in the following ways:

- Actin and myosin interact by the sliding filament mechanism.
- The final trigger for contraction is a rise in the intracellular calcium ion level.
- ATP energizes the sliding process.

During excitation-contraction coupling, the tubules of the SR release Ca^{2+} , but, as mentioned above, Ca^{2+} also moves into the cell from the extracellular space via membrane channels. In all striated muscle types, calcium ions activate myosin by binding to troponin. In smooth muscle, calcium activates myosin by interacting with a regulatory molecule called **calmodulin**, a cytoplasmic calcium-binding protein. Calmodulin, in turn, interacts with a kinase enzyme called **myosin kinase** or **myosin light chain kinase** which phosphorylates the myosin, activating it (Figure 9.28).

As in skeletal muscle, smooth muscle relaxes when intracellular Ca^{2+} levels drop—but getting smooth muscle to stop contracting is more complex. Events known to be involved include calcium detachment from calmodulin, active transport of Ca^{2+} into the SR and extracellular fluid, and dephosphorylation of myosin by a phosphatase enzyme, which reduces the activity of the myosin ATPases.

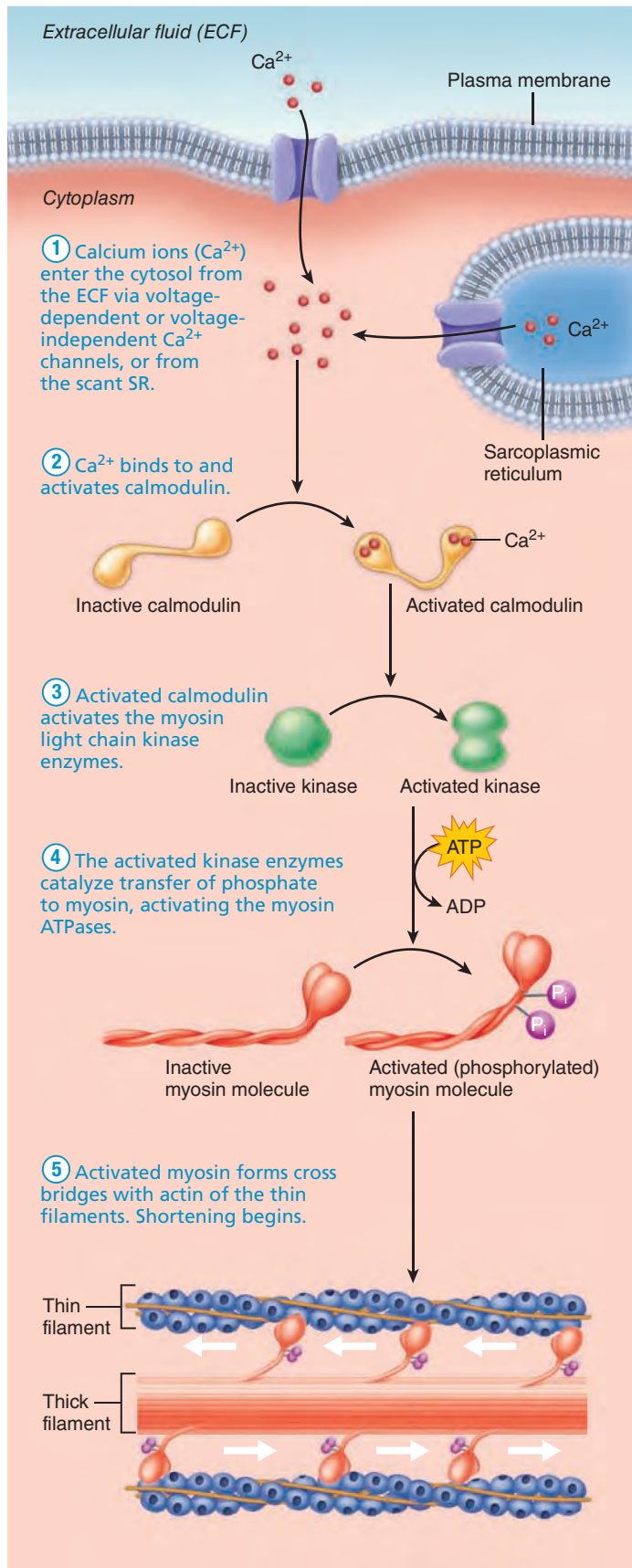


Figure 9.28 Sequence of events in excitation-contraction coupling of smooth muscle.

Energy Efficiency of Smooth Muscle Contraction

Smooth muscle takes 30 times longer to contract and relax than does skeletal muscle, but it can maintain the same contractile tension for prolonged periods at less than 1% of the energy cost. If skeletal muscle is like a speedy windup car that quickly runs down, then smooth muscle is like a steady, heavy-duty engine that lumbers along tirelessly.

Part of the striking energy economy of smooth muscle is the sluggishness of its ATPases compared to those in skeletal muscle. Moreover, smooth muscle myofilaments may latch together during prolonged contractions, saving energy in that way as well. Smooth muscle cells may maintain that *latch state* even after myosin is dephosphorylated.

The smooth muscle in small arterioles and other visceral organs routinely maintains a moderate degree of contraction, called *smooth muscle tone*, day in and day out without fatiguing. Smooth muscle has low energy requirements, and as a rule, it makes enough ATP via aerobic pathways to keep up with the demand.

Regulation of Contraction

The contraction of smooth muscle can be regulated by nerves, hormones, or local chemical changes. Let's briefly consider each of these methods.

Neural Regulation In some cases, the activation of smooth muscle by a neural stimulus is identical to that in skeletal muscle: Neurotransmitter binding generates an action potential, which is coupled to a rise in calcium ions in the cytosol. However, some types of smooth muscle respond to neural stimulation with graded potentials (local electrical signals) only.

Recall that all somatic nerve endings, that is, nerve endings that excite skeletal muscle, release the neurotransmitter acetylcholine. However, different autonomic nerves serving the smooth muscle of visceral organs release different neurotransmitters, each of which may excite or inhibit a particular group of smooth muscle cells.

The effect of a specific neurotransmitter on a smooth muscle cell depends on the type of receptor molecules on the cell's sarcolemma. For example, when acetylcholine binds to ACh receptors on smooth muscle in the bronchioles (small air passageways of the lungs), the response is strong contraction that narrows the bronchioles. When norepinephrine, released by a different type of autonomic nerve fiber, binds to norepinephrine receptors on the *same* smooth muscle cells, the effect is inhibitory—the muscle relaxes, which dilates the bronchioles. However, when norepinephrine binds to smooth muscle in the walls of most blood vessels, it stimulates the smooth muscle cells to contract and constrict the vessel.

Hormones and Local Chemical Factors Some smooth muscle layers have no nerve supply at all. Instead, they depolarize spontaneously or in response to chemical stimuli that bind to G protein-linked receptors. Other smooth muscle cells respond to both neural and chemical stimuli.

Several chemical factors cause smooth muscle to contract or relax without an action potential by enhancing or inhibiting

Ca²⁺ entry into the sarcoplasm. They include certain hormones, histamine, excess carbon dioxide, low pH, and lack of oxygen. The direct response to these chemical stimuli alters smooth muscle activity according to local tissue needs and probably is most responsible for smooth muscle tone. For example, the hormone gastrin stimulates stomach smooth muscle to contract so it can churn foodstuffs more efficiently. We will consider activation of smooth muscle in specific organs as we discuss each organ in subsequent chapters.

Special Features of Smooth Muscle Contraction

Smooth muscle is intimately involved in the functioning of most hollow organs and has a number of unique characteristics. We have already considered some of these—smooth muscle tone, slow prolonged contractions, and low energy requirements. But smooth muscle also responds differently to stretch and can lengthen and shorten more than other muscle types. Let's take a look.

Response to Stretch Up to a point, when skeletal muscle is stretched, it responds with more vigorous contractions. Stretching of smooth muscle also provokes contraction, which automatically moves substances along an internal tract. However, the increased tension persists only briefly, and soon the muscle adapts to its new length and relaxes, while still retaining the ability to contract on demand.

This **stress-relaxation response** allows a hollow organ to fill or expand slowly to accommodate a greater volume without causing strong contractions that would expel its contents. This is an important attribute, because organs such as the stomach and intestines must store their contents long enough to digest and absorb the nutrients. Likewise, your urinary bladder must be able to store the continuously made urine until it is convenient to empty your bladder, or you would spend all your time in the bathroom.

Length and Tension Changes Smooth muscle stretches much more and generates more tension than skeletal muscles stretched to a comparable extent. As we saw in Figure 9.22, precise, highly organized sarcomeres limit how far a skeletal muscle can stretch before it is unable to generate force.

In contrast, the irregular, overlapping arrangement of smooth muscle filaments and the lack of sarcomeres allow them to generate considerable force, even when they are substantially stretched. The total length change that skeletal muscles can undergo and still function efficiently is about 60% (from 30% shorter to 30% longer than resting length), but smooth muscle can contract when it is anywhere from half to twice its resting length—a total range of 150%. This capability allows hollow organs to tolerate tremendous changes in volume without becoming flabby when they empty.

Hyperplasia All muscle cells can hypertrophy (increase in cell size), but certain smooth muscle fibers can also undergo *hyperplasia*, that is, they divide to increase their numbers. Consider the response of the uterus to the hormone estrogen. At puberty, girls' blood estrogen levels rise. As estrogen binds to uterine smooth muscle receptors, it stimulates the synthesis of more

uterine smooth muscle, causing the uterus to grow to adult size. During pregnancy, high blood levels of estrogen stimulate uterine hyperplasia to accommodate the growing fetus.

Types of Smooth Muscle

The smooth muscle in different body organs varies substantially in its (1) fiber arrangement and organization, (2) innervation, and (3) responsiveness to various stimuli. For simplicity, however, smooth muscle is usually categorized into two major types: *unitary* and *multi unit*.

Unitary Smooth Muscle

Unitary smooth muscle, commonly called **visceral muscle** because it is in the walls of all hollow organs except the heart, is far more common. All the smooth muscle characteristics described so far pertain to unitary smooth muscle.

For example, the cells of unitary smooth muscle

- Are arranged in opposing (longitudinal and circular) sheets
- Are innervated by varicosities of autonomic nerve fibers and often exhibit rhythmic spontaneous action potentials
- Are electrically coupled by gap junctions and so contract as a unit (for this reason recruitment is not an option in unitary smooth muscle)
- Respond to various chemical stimuli

Multi Unit Smooth Muscle

The smooth muscles in the large airways to the lungs and in large arteries, the arrector pili muscles attached to hair follicles, and the internal eye muscles that adjust pupil size and allow the eye to focus visually are all examples of **multi unit smooth muscle**.

In contrast to unitary muscle, gap junctions and spontaneous depolarizations are rare. Like skeletal muscle, multi unit smooth muscle

- Consists of muscle fibers that are structurally independent of one another
- Is richly supplied with nerve endings, each of which forms a motor unit with a number of muscle fibers
- Responds to neural stimulation with graded contractions that involve recruitment

However, skeletal muscle is served by the somatic (voluntary) division of the nervous system. Multi unit smooth muscle, like unitary smooth muscle, is innervated by the autonomic (involuntary) division and also responds to hormones.

✓ Check Your Understanding

17. Compare the structures of skeletal and smooth muscle fibers.
18. Calcium is the trigger for contraction of all muscle types. How does its binding site differ in skeletal and smooth muscle fibers?
19. How does the stress-relaxation response suit the role of smooth muscle in hollow organs?

For answers, see Appendix H.

(Text continues on p. 312.)

Table 9.3 Comparison of Skeletal, Cardiac, and Smooth Muscle


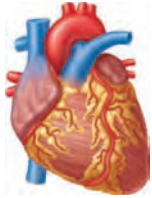

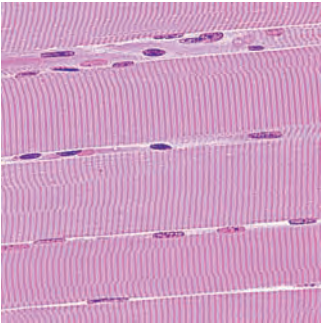

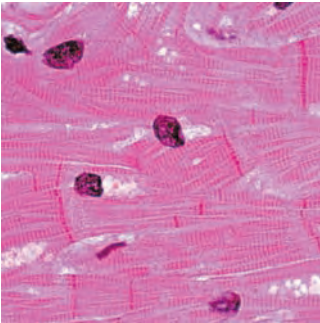

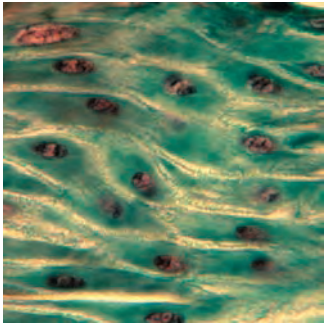

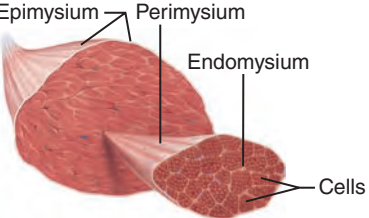
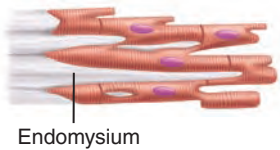
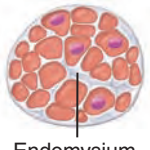
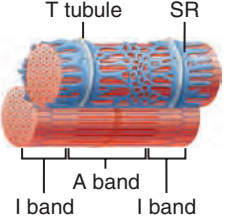
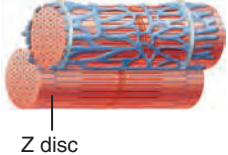

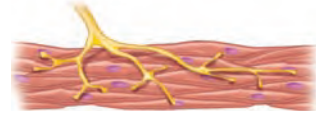
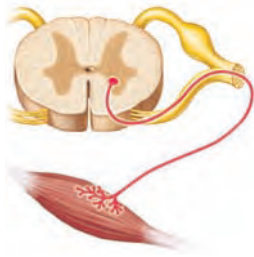
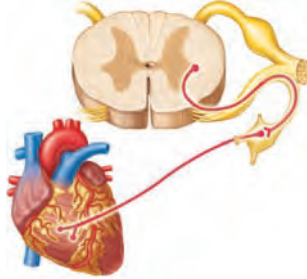
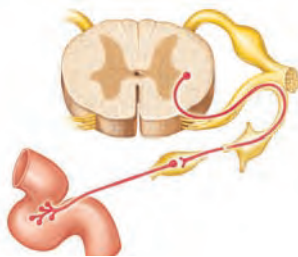
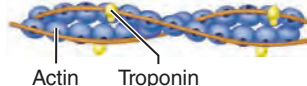
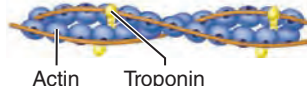
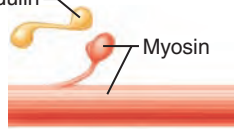

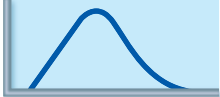
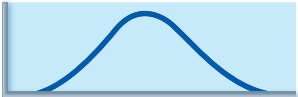
CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Body location	Attached to bones or (some facial muscles) to skin 	Walls of the heart 	Unitary muscle in walls of hollow visceral organs (other than the heart); multi unit muscle in intrinsic eye muscles, airways, large arteries 
Cell shape and appearance	Single, very long, cylindrical, multinucleate cells with obvious striations  	Branching chains of cells; uni- or binucleate; striations  	Single, fusiform, uninucleate; no striations  
Connective tissue components	Epimysium, perimysium, and endomysium 	Endomysium attached to fibrous skeleton of heart 	Endomysium 
Presence of myofibrils composed of sarcomeres	Yes	Yes, but myofibrils are of irregular thickness	No, but actin and myosin filaments are present throughout; dense bodies anchor actin filaments
Presence of T tubules and site of invagination	Yes; two in each sarcomere at A-I junctions 	Yes; one in each sarcomere at Z disc; larger diameter than those of skeletal muscle 	No; only caveolae

Table 9.3 (continued)

CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Elaborate sarcoplasmic reticulum	Yes	Less than skeletal muscle (1–8% of cell volume); scant terminal cisterns	Equivalent to cardiac muscle (1–8% of cell volume); some SR contacts the sarcolemma
Presence of gap junctions	No	Yes; at intercalated discs	Yes; in unitary muscle
Cells exhibit individual neuromuscular junctions	Yes	No	Not in unitary muscle; yes in multi-unit muscle
			
Regulation of contraction	Voluntary via axon terminals of the somatic nervous system	Involuntary; intrinsic system regulation; also autonomic nervous system controls; hormones; stretch	Involuntary; autonomic nerves, hormones, local chemicals; stretch
			
Source of Ca ²⁺ for calcium pulse	Sarcoplasmic reticulum (SR)	SR and from extracellular fluid	SR and from extracellular fluid
Site of calcium regulation	Troponin on actin-containing thin filaments	Troponin on actin-containing thin filaments	Calmodulin in the cytosol
			
Presence of pacemaker(s)	No	Yes	Yes (in unitary muscle only)
Effect of nervous system stimulation	Excitation	Excitation or inhibition	Excitation or inhibition
Speed of contraction	Slow to fast	Slow	Very slow
			
Rhythmic contraction	No	Yes	Yes in unitary muscle
Response to stretch	Contractile strength increases with degree of stretch (to a point)	Contractile strength increases with degree of stretch	Stress-relaxation response
Respiration	Aerobic and anaerobic	Aerobic	Mainly aerobic

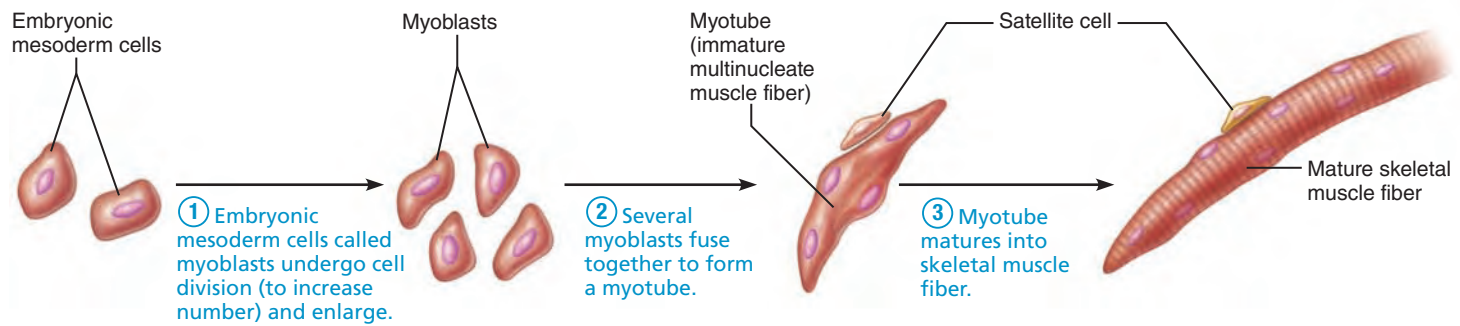


Figure 9.29 Myoblasts fuse to form a multinucleate skeletal muscle fiber.

Developmental Aspects of Muscles

- ✓ Describe embryonic development of muscle tissues and the changes that occur in skeletal muscles with age.

With rare exceptions, all three types of muscle tissue develop from embryonic mesoderm cells called **myoblasts**. In forming skeletal muscle tissue, several myoblasts fuse to form multinuclear *myotubes* (Figure 9.29). Integrins (cell adhesion proteins) in the myoblast membranes guide this process and soon functional sarcomeres appear. Skeletal muscle fibers are contracting by week 7 when the embryo is only about 2.5 cm (1 inch) long.

Initially, ACh receptors “sprout” over the entire surface of the developing myoblasts. As spinal nerves invade the muscle masses, the nerve endings target individual myoblasts and release the growth factor *agrin*. This chemical activates a muscle kinase (MuSK), which stimulates clustering and maintenance of ACh receptors at the newly forming neuromuscular junction in each muscle fiber. Then, the nerve endings release a different chemical that eliminates the receptor sites not innervated or stabilized by agrin.

Electrical activity in the neurons serving the muscle fibers also plays a critical role in muscle fiber maturation. As the somatic nervous system assumes control of muscle fibers, the number of fast and slow contractile fiber types is determined.

Myoblasts producing cardiac and smooth muscle cells do not fuse but develop gap junctions at a very early embryonic stage. Cardiac muscle is pumping blood just 3 weeks after fertilization. Specialized skeletal and cardiac muscle cells stop dividing early on but retain the ability to lengthen and thicken in a growing child and to hypertrophy in adults.

- **Satellite cells**, myoblast-like cells associated with skeletal muscle, help repair injured fibers and allow limited regeneration of dead skeletal muscle, a capability that declines with age.
- Cardiac muscle was thought to have no regenerative capability whatsoever, but recent studies suggest that cardiac cells do divide at a modest rate. Nonetheless, injured heart muscle is repaired mostly by scar tissue.
- Smooth muscles have a good regenerative capacity and smooth muscle cells of blood vessels divide regularly throughout life.

At birth, a baby’s movements are uncoordinated and largely reflexive. Muscular development reflects the level of neuromuscular coordination, which develops in a head-to-toe and proximal-to-

distal direction. In other words, a baby can lift its head before it can walk, and gross movements precede fine ones.

All through childhood, our control of our skeletal muscles becomes more and more sophisticated. By midadolescence, we reach the peak of our natural neural control of muscles, but can improve it by athletic or other types of training.

A frequently asked question is whether the strength difference between women and men has a biological basis. It does. Individuals vary, but on average, women’s skeletal muscles make up approximately 36% of body mass, whereas men’s account for about 42%. Men’s greater muscular development is due primarily to the effects of testosterone on skeletal muscle, not to the effects of exercise. Body strength per unit muscle mass, however, is the same in both sexes. Strenuous muscle exercise causes more muscle enlargement in males than in females, again because of the influence of testosterone. Some athletes take large doses of synthetic male sex hormones (“steroids”) to increase their muscle mass. *A Closer Look* discusses this illegal and physiologically dangerous practice.

Because of its rich blood supply, skeletal muscle is amazingly resistant to infection. Given good nutrition and moderate exercise, relatively few problems afflict skeletal muscles. However, muscular dystrophy, the world’s most common genetic disorder, is a serious condition that deserves more than a passing mention.

Homeostatic Imbalance 9.4

The term **muscular dystrophy** refers to a group of inherited muscle-destroying diseases that generally appear during childhood. The affected muscles initially enlarge due to deposits of fat and connective tissue, but the muscle fibers atrophy and degenerate.

The most common and serious form is **Duchenne muscular dystrophy (DMD)**, which is inherited as a sex-linked recessive disease. It is expressed almost exclusively in males (one in every 3600 male births). This tragic disease is usually diagnosed when the boy is between 2 and 7 years old. Active, normal-appearing children become clumsy and fall frequently as their skeletal muscles weaken. The disease progresses relentlessly from the extremities upward, finally affecting the head and chest muscles and cardiac muscle. Victims rarely live beyond their early 20s, dying of respiratory failure.

DMD is caused by a defective gene for *dystrophin*, a cytoplasmic protein that links the cytoskeleton to the extracellular matrix and, like a girder, helps stabilize the sarcolemma. The fragile sarcolemma of DMD patients tears during contraction, allowing entry of excess Ca^{2+} . The deranged calcium homeostasis damages

Athletes Looking Good and Doing Better with Anabolic Steroids?

Society loves a winner and top **athletes** reap large social and monetary rewards. It is not surprising that some will grasp at anything that might increase their **performance**—including “juice,” or anabolic **steroids**.

These drugs are variants of the male sex hormone **testosterone** engineered by pharmaceutical companies. They were introduced in the 1950s to treat anemia and certain muscle-wasting diseases and to prevent muscle atrophy in patients immobilized after surgery. Testosterone is responsible for the increase in muscle and bone mass and other physical changes that occur during puberty and converts boys into men.

Convinced that megadoses of steroids could produce enhanced masculinizing effects in grown men, many athletes and bodybuilders were using them by the early 1960s, a practice that is still going on. Investigations have stunned sports fans with revelations of steroid use by many elite athletes including Barry Bonds, formerly of the San Francisco Giants; Mark McGwire, formerly with the St. Louis Cardinals; and Marion Jones, one of the most celebrated women athletes of all time.

However, steroid use is not confined to professional athletes. It is estimated that nearly one in every 10 young men has tried them, and their use is also spreading among young women.

It is difficult to determine the extent of anabolic steroid use because most international competitions ban the use of drugs. Users (and prescribing physicians or drug dealers) are naturally reluctant to talk about it, and users stop doping before the event, aware that evidence of drug use is hard to find a week after they stop. Additionally, “underground” suppliers of performance-enhancing drugs keep producing new versions of designer steroids that evade standard antidoping tests. The Olympic Analytical Laboratory in Los Angeles

rocked the sports world when it revealed that a number of elite athletes tested positive for tetrahydrogestrinone (THG), a designer steroid not previously known or tested for.

There is little question that many professional bodybuilders and athletes competing in events that require muscle strength (e.g., shot put, discus throwing, and weight lifting) are heavy users. Football players have also admitted using steroids as an adjunct to training, diet, and psychological preparation for games. These athletes claim that anabolic steroids enhance muscle mass and strength, and raise oxygen-carrying capability owing to greater volume of red blood cells.

Typically, bodybuilders who use steroids combine high doses (up to 200 mg/day) via injection or transdermal skin patches with heavy resistance training. Intermittent use begins several months before an event, and commonly entails taking many anabolic steroid supplements (a method called stacking). They increase doses gradually as the competition nears.

Do the drugs do all that is claimed? Research studies report increased isometric strength and body weight in steroid users. While these are results weight lifters dream about, for runners and others requiring fine muscle coordination and endurance these changes may not translate into better performance. The “jury is still out” on this question.

Do the alleged advantages of steroids outweigh their risks? Absolutely not. Anabolic steroids cause: bloated faces (Cushingoid sign of steroid excess), acne and hair loss, shriveled testes and infertility, liver damage that promotes liver cancer, and changes in blood cholesterol levels that may predispose users to heart disease.

In addition, females can develop masculine characteristics such as smaller breasts, enlarged clitoris, excess body hair, and thinning scalp hair. The psychiatric



hazards of anabolic steroid use may be equally threatening: Recent studies indicate that one-third of users suffer serious mental problems. Depression, delusions, and manic behavior—in which users undergo Jekyll-and-Hyde personality swings and become extremely violent (termed *roid rage*)—are all common.

Another recent arrival on the scene, sold over the counter as a “nutritional performance-enhancer,” is androstenedione, which is converted to testosterone in the body. Though it is taken orally (and the liver destroys much of it soon after ingestion), the few milligrams that survive temporarily boost testosterone levels. Reports of athletic wannabes from the fifth grade up sweeping the supplement off the drugstore shelves are troubling, particularly since it is not regulated by the U.S. Food and Drug Administration (FDA) and its long-term effects are unknown.

A study at Massachusetts General Hospital found that males who took androstenedione developed higher levels of the female hormone estrogen as well as testosterone, raising their risk of feminizing effects such as enlarged breasts. Youths with elevated levels of estrogen or testosterone may enter puberty early, stunting bone growth and leading to shorter-than-normal adult height.

Some people seem willing to try almost anything to win, short of killing themselves. Are they unwittingly doing this as well?

the contractile fibers, and inflammatory cells (macrophages and lymphocytes) accumulate in the surrounding connective tissue. As the regenerative capacity of the muscle is lost, and damaged cells undergo apoptosis, muscle mass drops.

There is still no cure for DMD. Current treatments are aimed at preventing or reducing spine and joint deformities and helping those with DMD remain mobile as long as possible. Thus far the only medication that has improved muscle strength and func-

tion is the steroid prednisone, but other immunosuppressant drugs may delay muscle deterioration.

One initially promising technique, *myoblast transfer therapy* (injecting healthy myoblast cells that fuse with diseased myoblasts) has been disappointing. Newer experimental therapies have reversed disease symptoms in dystrophic animal models. One of these involves injection of adeno-associated viruses carrying pared-down microdystrophin genes. A different approach

Homeostatic Interrelationships Between the Muscular System and Other Body Systems



9

Integumentary System Chapter 5

- Muscular exercise enhances circulation to skin and improves skin health
- Skin protects the muscles by external enclosure; helps dissipate heat generated by the muscles

Skeletal System Chapters 6–8

- Skeletal muscle activity maintains bone health and strength
- Bones provide levers for muscle activity

Nervous System Chapters 11–15

- Facial muscle activity allows emotions to be expressed
- Nervous system stimulates and regulates muscle activity
- Nervous system activity maintains muscle mass

Endocrine System Chapter 16

- Growth hormone and androgens influence skeletal muscle strength and mass; other hormones help regulate cardiac and smooth muscle activity

Cardiovascular System Chapters 17–19

- Skeletal muscle activity increases efficiency of cardiovascular functioning; helps prevent atherosclerosis and causes cardiac hypertrophy
- Cardiovascular system delivers needed oxygen and nutrients to muscles

Lymphatic System/Immunity Chapters 20–21

- Physical exercise may enhance or depress immunity depending on its intensity
- Lymphatic vessels drain leaked tissue fluids; immune system protects muscles from disease

Respiratory System Chapter 22

- Muscular exercise increases respiratory capacity and efficiency of gas exchange
- Respiratory system provides oxygen and disposes of carbon dioxide

Digestive System Chapter 23

- Physical activity increases gastrointestinal motility and elimination when at rest
- Digestive system provides nutrients needed for muscle health; liver metabolizes lactic acid

Urinary System Chapters 25–26

- Physical activity promotes normal voiding behavior; skeletal muscle forms the voluntary sphincter of the urethra
- Urinary system disposes of nitrogenous wastes

Reproductive System Chapter 27

- Skeletal muscle helps support pelvic organs (e.g., uterus); assists erection of penis and clitoris
- Testicular androgen promotes increased skeletal muscle

being tested is coaxing dystrophic muscles to produce more *utrophin*, a similar protein present in low amounts in adults but at much higher levels in fetal muscles. In mice at least, utrophin can compensate for dystrophin deficiency. +

As we age, the amount of connective tissue in our skeletal muscles increases, the number of muscle fibers decreases, and the muscles become stringier, or more sinewy. By age 30, even in healthy people, a gradual loss of muscle mass, called *sarcopenia* (sar-co-pe'ne-ah), begins. Apparently the same regulatory molecules (transcription factors, enzymes, hormones, and others) that promote muscle growth also oversee this type of muscle atrophy. Because skeletal muscles form so much of the body mass, body weight and muscle strength decline in tandem. By age 80, muscle strength usually decreases by about 50%. This “flesh wasting” condition has serious health implications for the elderly, particularly because falling becomes a common event.

Muscles can also suffer indirectly. Aging of the cardiovascular system affects nearly every organ in the body, and muscles are no exception. As atherosclerosis takes its toll and begins to block distal arteries, a circulatory condition called *intermittent claudication* (klaw'di-ka'shun; “limping”) occurs in some individuals. This condition restricts blood delivery to the legs, leading to excruciating pains in the leg muscles during walking, which forces the person to stop and rest.

But we don't have to slow up during old age. Regular exercise helps reverse sarcopenia, and frail elders who begin to “pump iron” (lift leg and hand weights) can rebuild muscle mass and dramatically increase their strength. Performing those lifting exercises rapidly can improve our ability to carry out the

“explosive” movements needed to rise from a chair. Even moderate activity, like taking a walk daily, improves neuromuscular function and enhances independent living.

Smooth muscle is remarkably trouble free. Most problems that impair gastrointestinal function, for instance, stem from irritants such as excess alcohol, spicy foods, or bacterial infection. Under such conditions, smooth muscle motility increases in an attempt to rid the body of irritating agents, and diarrhea or vomiting occur.

✓ Check Your Understanding

20. How is the multinucleate condition achieved during development of skeletal muscle fibers?
21. What does it mean when we say “muscles get stringier with age”?
22. How can we defer (or reverse) some of the effects of age on skeletal muscles?

For answers, see Appendix H.

The capacity for movement is a property of all cells but, with the exception of muscle, these movements are largely restricted to intracellular events. Skeletal muscles, the major focus of this chapter, permit us to interact with our external environment in an amazing number of ways, and they also contribute to our internal homeostasis as summarized in *System Connections*.

In this chapter we have covered muscle anatomy from gross to molecular levels and have considered muscle physiology in some detail. Chapter 10 continues from this point to explain how skeletal muscles interact with bones and with each other, and then describes the individual skeletal muscles that make up the muscular system of the body.

Chapter Summary



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Overview of Muscle Tissues (pp. 276–278)

Types of Muscle Tissue (p. 277)

1. Skeletal muscle is attached to the skeleton, is striated, and can be controlled voluntarily.
2. Cardiac muscle forms the heart, is striated, and is controlled involuntarily.
3. Smooth muscle, located chiefly in the walls of hollow organs, is controlled involuntarily. Its fibers are not striated.

Special Characteristics of Muscle Tissue (p. 277)

4. Special functional characteristics of muscle include excitability, contractility, extensibility, and elasticity.

Muscle Functions (pp. 277–278)

5. Muscles move internal and external body parts, maintain posture, stabilize joints, generate heat, and protect some visceral organs.

Skeletal Muscle (pp. 278–305)

Gross Anatomy of a Skeletal Muscle (pp. 278–279)

1. Connective tissue coverings protect and strengthen skeletal muscle fibers (cells). Superficial to deep, these are epimysium, perimysium, and endomysium.
2. Skeletal muscle attachments (origins/insertions) may be direct or indirect via tendons or aponeuroses. Indirect attachments withstand friction better.

Microscopic Anatomy of a Skeletal Muscle Fiber (pp. 279–285)

3. Skeletal muscle fibers are long, striated, and multinucleate.
4. Myofibrils are contractile elements that occupy most of the cell volume. Their banded appearance results from a regular alternation of dark (A) and light (I) bands. Myofibrils are chains of sarcomeres; each sarcomere contains thick (myosin) and thin (actin) myofilaments arranged in a regular array. The heads of myosin molecules form cross bridges that interact with the thin filaments.
5. The sarcoplasmic reticulum (SR) is a system of membranous tubules surrounding each myofibril. Its function is to release and then sequester calcium ions.

6. T tubules are invaginations of the sarcolemma that run between the terminal cisterns of the SR. They allow an electrical stimulus to be delivered quickly deep into the cell.

Sliding Filament Model of Contraction (p. 285)

7. According to the sliding filament model, cross bridge (myosin head) activity of the thick filaments pulls the thin filaments toward the sarcomere centers.

Physiology of Skeletal Muscle Fibers (pp. 285–293)

8. Regulation of skeletal muscle cell contraction involves (a) generating and transmitting an action potential along the sarcolemma and (b) excitation-contraction coupling.
9. An end plate potential is set up when acetylcholine released by a nerve ending binds to ACh receptors on the sarcolemma, causing local changes in membrane permeability which allow ion flows that depolarize the membrane at that site.
10. The flow of current from the locally depolarized area spreads to the adjacent area of the sarcolemma, opening voltage-gated Na^+ channels, which allows Na^+ influx. These events generate the action potential. Once initiated, the action potential is self-propagating and unstoppable.
11. Then as the action potential travels away from a region, Na^+ channels close and voltage-gated K^+ channels open, repolarizing the membrane.
12. In excitation-contraction coupling the action potential is propagated down the T tubules, causing calcium to be released from the SR into the cytosol.
13. Sliding of the filaments is triggered by a rise in intracellular calcium ion levels. Troponin binding of calcium moves tropomyosin away from myosin-binding sites on actin, allowing cross bridge binding. Myosin ATPases split ATP, which energizes the power strokes. ATP binding to the myosin head is necessary for cross bridge detachment. Cross bridge activity ends when calcium is pumped back into the SR.

iP Muscular System; Topic: Sliding Filament Theory, pp. 18–29.

Contraction of a Skeletal Muscle (pp. 293–298)

14. A motor unit is one motor neuron and all the muscle cells it innervates. The neuron's axon has several branches, each of which forms a neuromuscular junction with one muscle cell.
15. A motor unit's response to a single brief threshold stimulus is a twitch. A twitch has three phases: latent (preparatory events occurring), contraction (the muscle tenses and may shorten), and relaxation (muscle tension declines and the muscle returns to its resting length).
16. Graded responses of muscles to rapid stimuli are wave summation and unfused and fused tetanus. A graded response to increasingly strong stimuli is multiple motor unit summation, or recruitment. The type and order of motor unit recruitment follows the size principle.
17. Isotonic contractions occur when the muscle shortens (concentric contraction) or lengthens (eccentric contraction) as the load is moved. Isometric contractions occur when muscle tension produces neither shortening nor lengthening.

iP Muscular System; Topic: Contraction of Motor Units, pp. 1–11.

Muscle Metabolism (pp. 298–301)

18. The energy source for muscle contraction is ATP, obtained from a coupled reaction of creatine phosphate with ADP and from aerobic and anaerobic metabolism of glucose.
19. When ATP is produced by anaerobic pathways, lactic acid accumulates and ionic imbalances disturb the membrane potential. To return the muscles to their resting state, ATP must be produced

aerobically and used to regenerate creatine phosphate, glycogen reserves must be restored, and accumulated lactic acid must be metabolized. Oxygen used to accomplish this repayment is called excess postexercise oxygen consumption (EPOC).

20. Only about 40% of energy released during ATP hydrolysis powers contractile activity. The rest is liberated as heat.

iP Muscular System; Topic: Muscle Metabolism, pp. 1–7.

Force of Muscle Contraction (pp. 301–302)

21. The force of muscle contraction is affected by the number and size of contracting muscle cells (the more and the larger the cells, the greater the force), the frequency of stimulation, and the degree of muscle stretch.
22. In twitch contractions, the external tension exerted on the load is always less than the internal tension. When a muscle is tetanized, the external tension equals the internal tension.
23. When the thick and thin filaments are optimally overlapping, the muscle can generate maximum force. With excessive increase or decrease in muscle length, force declines.

Velocity and Duration of Contraction (pp. 302–304)

24. Factors determining the velocity and duration of muscle contraction include the load (the greater the load, the slower the contraction) and muscle fiber types.
25. The three types of muscle fibers are: (1) fast glycolytic (fatigable) fibers, (2) slow oxidative (fatigue-resistant) fibers, and (3) fast oxidative (fatigue-resistant) fibers. Most muscles contain a mixture of fiber types. The fast muscle fiber types can interconvert with certain exercise regimens.

Adaptations to Exercise (pp. 304–305)

26. Regular aerobic exercise gives skeletal muscles increased efficiency, endurance, strength, and resistance to fatigue.
27. In skeletal muscle, resistance exercises cause hypertrophy and large gains in strength.
28. Immobilizing muscles leads to muscle weakness and severe atrophy.
29. Improper training and excessive exercise result in overuse injuries, which may be disabling.

Smooth Muscle (pp. 305–311)

Microscopic Structure of Smooth Muscle Fibers (pp. 305–307)

1. A smooth muscle fiber is spindle shaped and uninucleate, and has no striations.
2. Smooth muscle cells are most often arranged in sheets. They lack elaborate connective tissue coverings.
3. The SR is poorly developed and T tubules are absent. Actin and myosin filaments are present, but sarcomeres are not. Intermediate filaments and dense bodies form an intracellular network that harnesses the pull generated during cross bridge activity and transfers it to the extracellular matrix.

Contraction of Smooth Muscle (pp. 307–309)

4. Smooth muscle fibers may be electrically coupled by gap junctions.
5. ATP energizes smooth muscle contraction, which is activated by a calcium pulse. However, calcium binds to calmodulin rather than to troponin (which is not present in smooth muscle fibers), and myosin must be phosphorylated to become active in contraction.
6. Smooth muscle contracts for extended periods at low energy cost and without fatigue.
7. Neurotransmitters of the autonomic nervous system may inhibit or stimulate smooth muscle fibers. Smooth muscle contraction may also be initiated by pacemaker cells, hormones, or local chemical factors that influence intracellular calcium levels, and by mechanical stretch.

8. Special features of smooth muscle contraction include the stress-relaxation response, the ability to generate large amounts of force when extensively stretched, and hyperplasia under certain conditions.

Types of Smooth Muscle (p. 309)

9. Unitary smooth muscle has electrically coupled fibers that contract synchronously and often spontaneously.
10. Multi unit smooth muscle has independent, well-innervated fibers that lack gap junctions and pacemaker cells. Stimulation occurs via autonomic nerves (or hormones). Multi unit muscle contractions are rarely synchronous.

Developmental Aspects of Muscles (pp. 312–313, 315)

1. Muscle tissue develops from embryonic mesoderm cells called myoblasts. Several myoblasts fuse to form a skeletal muscle fiber.

Smooth and cardiac cells develop from single myoblasts and display gap junctions.

2. For the most part, specialized skeletal and cardiac muscle cells lose their ability to divide but retain the ability to hypertrophy. Smooth muscle regenerates well and undergoes hyperplasia.
3. Skeletal muscle development reflects maturation of the nervous system and occurs in head-to-toe and proximal-to-distal directions. Natural neuromuscular control reaches its peak in midadolescence.
4. Women's muscles account for about 36% of their total body weight and men's for about 42%, a difference due chiefly to the effects of male hormones on skeletal muscle growth.
5. Skeletal muscle is richly vascularized and quite resistant to infection, but in old age, skeletal muscles become fibrous, decline in strength, and atrophy. Regular exercise can offset some of these changes.

Review Questions

Multiple Choice/Matching

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

- The connective tissue covering that encloses the sarcolemma of an individual muscle fiber is called the (a) epimysium, (b) perimysium, (c) endomysium, (d) periosteum.
- A fascicle is a (a) muscle, (b) bundle of muscle fibers enclosed by a connective tissue sheath, (c) bundle of myofibrils, (d) group of myofilaments.
- Thick and thin myofilaments have different compositions. For each descriptive phrase, indicate whether the filament is (a) thick or (b) thin.
 - ___ (1) contains actin
 - ___ (2) contains ATPases
 - ___ (3) attaches to the Z disc
 - ___ (4) contains myosin
 - ___ (5) contains troponin
 - ___ (6) does not lie in the I band
- The function of the T tubules in muscle contraction is to (a) make and store glycogen, (b) release Ca^{2+} into the cell interior and then pick it up again, (c) transmit the action potential deep into the muscle cells, (d) form proteins.
- The sites where the motor nerve impulse is transmitted from the nerve endings to the skeletal muscle cell membranes are the (a) neuromuscular junctions, (b) sarcomeres, (c) myofilaments, (d) Z discs.
- Contraction elicited by a single brief stimulus is called (a) a twitch, (b) wave summation, (c) multiple motor unit summation, (d) fused tetanus.
- A smooth, sustained contraction resulting from very rapid stimulation of the muscle, in which no evidence of relaxation is seen, is called (a) a twitch, (b) wave summation, (c) multiple motor unit summation, (d) fused tetanus.
- Characteristics of isometric contractions include all but (a) shortening, (b) increased muscle tension throughout the contraction phase, (c) absence of shortening, (d) used in resistance training.
- During muscle contraction, ATP is provided by (a) a coupled reaction of creatine phosphate with ADP, (b) aerobic respiration of glucose, and (c) anaerobic glycolysis.
 - ___ (1) Which provides ATP fastest?
 - ___ (2) Which does (do) not require that oxygen be available?

___ (3) Which provides the highest yield of ATP per glucose molecule?

___ (4) Which results in the formation of lactic acid?

___ (5) Which has carbon dioxide and water products?

___ (6) Which is most important in endurance sports?

- The neurotransmitter released by somatic motor neurons is (a) acetylcholine, (b) acetylcholinesterase, (c) norepinephrine.
- The ions that enter the skeletal muscle cell during the generation of an action potential are (a) calcium ions, (b) chloride ions, (c) sodium ions, (d) potassium ions.
- Myoglobin has a special function in muscle tissue. It (a) breaks down glycogen, (b) is a contractile protein, (c) holds a reserve supply of oxygen in the muscle.
- Aerobic exercise results in all of the following except (a) increased cardiovascular system efficiency, (b) more mitochondria in the muscle cells, (c) increased size and strength of existing muscle cells, (d) increased neuromuscular system coordination.
- The smooth muscle type found in the walls of digestive and urinary system organs and that exhibits gap junctions and pacemaker cells is (a) multi unit, (b) unitary.

Short Answer Essay Questions

- Name and describe the four special functional abilities of muscle that are the basis for muscle response.
- Distinguish between (a) direct and indirect muscle attachments and (b) a tendon and an aponeurosis.
- (a) Describe the structure of a sarcomere and indicate the relationship of the sarcomere to myofilaments. (b) Explain the sliding filament model of contraction using appropriately labeled diagrams of a relaxed and a contracted sarcomere.
- What is the importance of acetylcholinesterase in muscle cell contraction?
- Explain how a slight (but smooth) contraction differs from a vigorous contraction of the same muscle. Use the concepts of multiple motor unit summation.
- Explain what is meant by the term excitation-contraction coupling.
- Define and draw a motor unit.
- Describe the three distinct types of skeletal muscle fibers.
- True or false: Most muscles contain a predominance of one skeletal muscle fiber type. Explain the reasoning behind your choice.
- Describe some cause(s) of muscle fatigue and define this term clearly.

- Define EPOC.
- Smooth muscle has some unique properties, such as low energy usage, and the ability to maintain contraction over long periods. Tie these properties to the function of smooth muscle in the body.



Critical Thinking and Clinical Application Questions

- Jim Fitch decided that his physique left much to be desired, so he joined a local health club and began to “pump iron” three times weekly. After three months of training, during which he lifted increasingly heavier weights, he noticed that his arm and chest muscles were substantially larger. Explain the structural and functional basis of these changes.
- When a suicide victim was found, the coroner was unable to remove the drug vial clutched in his hand. Explain the reasons for this. If the victim had been discovered three days later, would the coroner have had the same difficulty? Explain.
- Muscle-relaxing drugs are administered to a patient during major surgery. Which of the two chemicals described next would be a good skeletal muscle relaxant and why?
 - Chemical A binds to and blocks ACh receptors of muscle cells.
 - Chemical B floods the muscle cells’ cytoplasm with Ca^{2+} .
- Michael is answering a series of questions dealing with skeletal muscle cell excitation and contraction. In response to “What protein changes shape when Ca^{2+} binds to it?” he writes “tropomyosin.” What should he have responded and what is the result of that calcium ion binding?

AT THE CLINIC

9

Related Clinical Terms

Fibromyositis (*fibro* = fiber; *itis* = inflammation) Also known as **fibromyalgia**; a group of conditions involving chronic inflammation of a muscle, its connective tissue coverings and tendons, and capsules of nearby joints. Symptoms are nonspecific and involve varying degrees of tenderness associated with specific trigger points, as well as fatigue and frequent awakening from sleep.

Hernia Protrusion of an organ through its body cavity wall. May be congenital (owing to failure of muscle fusion during development), but most often is caused by heavy lifting or obesity and subsequent muscle weakening.

Myalgia (mi-al’je-ah; *algia* = pain) Muscle pain resulting from any muscle disorder.

Myofascial pain syndrome Pain caused by a tightened band of muscle fibers, which twitch when the skin over them is touched. Mostly associated with overused or strained postural muscles.

Myopathy (mi-op’ah-the; *path* = disease, suffering) Any disease of muscle.

Myotonic dystrophy A form of muscular dystrophy that is less common than DMD; in the U.S. it affects about 14 of 100,000 people. Symptoms include a gradual reduction in muscle mass and control of the skeletal muscles, abnormal heart rhythm, and diabetes mellitus. May appear at any time; not sex-linked. Underlying genetic defect is multiple repeats of a particular gene

on chromosome 19. Because the number of repeats tends to increase from generation to generation, subsequent generations develop more severe symptoms. No effective treatment.

RICE Acronym for rest, ice, compression, and elevation. The standard treatment for a pulled muscle, or excessively stretched tendons or ligaments.

Spasm A sudden, involuntary twitch in smooth or skeletal muscle ranging from merely irritating to very painful; may be due to chemical imbalances. In spasms of the eyelid or facial muscles, called tics, psychological factors may be involved. Stretching and massaging the affected area may help end the spasm. A cramp is a prolonged spasm; usually occurs at night or after exercise.

Strain Commonly called a “pulled muscle,” a strain is excessive stretching and possible tearing of a muscle due to muscle overuse or abuse. The injured muscle becomes painfully inflamed (myositis), and adjacent joints are usually immobilized.

Tetanus (1) A state of sustained contraction of a muscle that is a normal aspect of skeletal muscle functioning. (2) An acute infectious disease caused by the anaerobic bacterium *Clostridium tetani* and resulting in persistent painful spasms of some skeletal muscles. Progresses to fixed rigidity of the jaws (lockjaw) and spasms of trunk and limb muscles. Usually fatal due to respiratory failure.



Case Study Muscular System

Let’s continue our tale of Mrs. DeStephano’s medical problems, this time looking at the notes made detailing observations of her skeletal musculature.

- Severe lacerations of the muscles of the right leg and knee
- Damage to the blood vessels serving the right leg and knee
- Transection of the sciatic nerve (the large nerve serving most of the lower limb), just above the right knee

Her physician orders daily passive range-of-motion (ROM) exercise and electrical stimulation for her right leg and a diet high in protein, carbohydrates, and vitamin C.

- Describe the step-by-step process of wound healing that will occur in her fleshy (muscle) wounds, and note the consequences of the specific restorative process that occurs.
- What complications in healing can be anticipated owing to vascular (blood vessel) damage in the right leg?
- What complications in muscle structure and function result from transection of the sciatic nerve? Why are passive ROM and electrical stimulation of her right leg muscles ordered?
- Explain the reasoning behind the dietary recommendations.

(Answers in Appendix H)